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# THE JOURNAL OF PEDIATRICS

A MONTHLY JOURNAL DEVOTED TO THE PROBLEMS AND DISEASES OF INFANCY AND CHILDHOOD

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# *The JOURNAL of PEDIATRICS*

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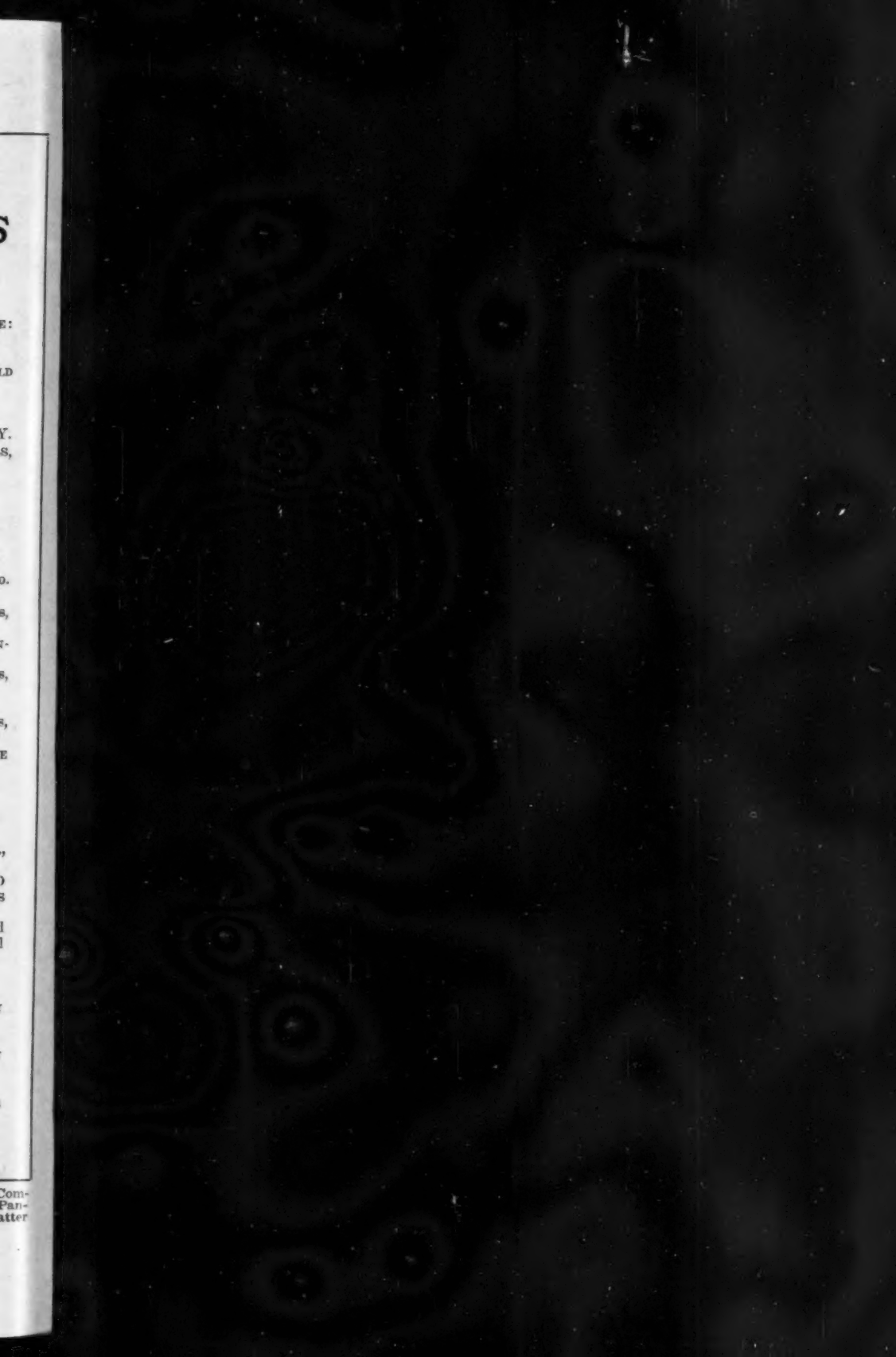

# The Journal of Pediatrics

VOL. 9 AUGUST, 1936 No. 2


## Original Communications

### TREATMENT OF NINETEEN CASES OF TYPHOID FEVER IN CHILDREN

#### WITH A REPORT ON THE IMPORTANCE OF NONSPECIFIC IMMUNOTRANSFUSION THERAPY


KARL HABEL, M.D., AND WALTER J. CROCKER, V.M.D.
PHILADELPHIA, PA.


THE purpose of this paper is to report the treatment of nineteen cases of typhoid fever in children under twelve years of age who were admitted to the Children's Department of the Philadelphia General Hospital during an epidemic of the disease, and particularly to record the rapid recovery of five very severe cases of typhoid fever in children following nonspecific immunotransfusion therapy.

In Philadelphia during June, 1935, an epidemic of typhoid fever resulted in the admission of ninety-two patients to the various hospitals of the city. Since all patients came from the same district, the Department of Public Health traced the source of infection to potato salad served at a picnic held within the city limits May 30.

Cultures of the drinking water at the picnic grounds were negative for typhoid bacilli. Two patients who had not attended the affair became ill after eating potato salad brought to them from the picnic by neighbors. Through this fact the carrier was identified as the individual who had prepared the salad.

#### ONSET AND SYMPTOMS

The nineteen children who were admitted to the Philadelphia General Hospital during the epidemic were definitely exposed at the same time, yet the incubation period varied from ten to twenty-three days. Fever was the first symptom noticed by the parents in most of the children. In the beginning fever was accompanied by no symptoms other than malaise and anorexia. In six individuals these three complaints were the only symptoms of importance during their illness before admission


From the Children's Department and Division of Clinical Pathology of the Laboratories of Philadelphia General Hospital.

Read before the Second Annual Meeting of Region I of the American Academy of Pediatrics, Philadelphia, Oct. 12, 1935.

to the hospital. Fainting or sudden dizziness, as the initial symptom, occurred in six female patients. As definite complaints anorexia occurred in eleven and malaise in eight patients. Of the cardinal symptoms headache was the most frequent, being present in ten cases, diarrhea in four, epistaxis in three, and melena in none.

### PHYSICAL EXAMINATION

The physical findings were more classical and made the diagnosis quite definite in this series of patients. All individuals showed rose spots on admission or a few days later, and approximately half of them subsequently developed new crops of rose spots. Eighteen patients showed the typical appearance of the tongue. It was coated on the dorsum and clean on the edges and tip. Abdominal distention was present in thirteen individuals. It was slight in the majority and marked in only a few patients. The spleen was palpable in twelve instances. Anterior and posterior cervical lymphadenopathy was noticeable in four patients. There was generalized tenderness on abdominal palpation in three cases. Bronchitis and dicrotic pulse were each found in two instances.

### LABORATORY FINDINGS

Laboratory proof of the disease was found in all of the patients. Blood cultures were positive for typhoid bacilli in fifteen individuals. Positive Widal reactions were obtained in the four cases which showed negative blood cultures. The Widal reactions varied greatly. The dilutions showing agglutination ranged from 0 to 1 to 1,280, although the patients were exposed at the same time and the Widal tests were done at the same stage of the disease. There was no correlation between the severity of the clinical symptoms and the grade of the Widal reactions.

Urine cultures were positive in only one patient, and all of the feces cultures were negative. Blood cultures and Widal tests could not be followed during the course of the disease, and urine and feces cultures were done only on admission and prior to discharge because of the large number of typhoid fever patients in both the adult and children's wards.

The leucocyte counts were low in most instances. The highest count was 15,400 in one patient while fifteen were below 10,000. The highest neutrophile count was 76 per cent, and twelve individuals showed a relative lymphocytosis.

### COURSE

The course of the disease in this series of patients was mild in general. The degree of toxicity was graded from 1+ to 5+, based on the duration of fever, amount of abdominal distention, degree of malaise and anorexia, occurrence of vomiting and diarrhea and the extent of the hemogramic left shift. Degrees of toxicity were as follows:

| | |
|---|---|
| 4 patients 1+ | 4 patients 4+ |
| 4 patients 2+ | 1 patient 5+ |
| 6 patients 3+ | |

The manifestations of toxicity were present only while the fever continued, although several patients showed very few toxic signs even while running high continuous temperatures. The duration of fever after admission is, we believe, a fair indication of the distribution of the severity of the infection. Days of fever were:

| | | | |
|---|---|---|---|
| 6 patients | 0-10 days | 1 patient | 30-40 days |
| 10 patients | 10-20 days | 0 patient | 40-50 days |
| 1 patient | 20-30 days | 1 patient | 50-60 days. |

Four patients had relapses, and only one ended her illness by becoming a carrier.

The details of the hospital course of the more severe cases are considered under the heading of treatment.

## TREATMENT

Nineteen children of approximately the same age, infected at the same source at the same time, offered an excellent opportunity for comparing results of different types of therapy. All patients were given the usual high caloric diet therapy.

Six patients were treated with a specific immune human serum intramuscularly, under the supervision of Dr. Stuart Mudd, of the University of Pennsylvania Hospital, and Dr. Aims McGuiness, of the Children's Hospital of Philadelphia, a detailed report of which they will probably present at a later time.

Briefly, the blood serum was obtained from adults who had been immunized ten days previously with the standard United States Army typhoid vaccine and was found to have an average titer of 1 to 300 by the Widal agglutination test. Patients showing various degrees of toxicity were selected, and the quantity and the frequency of administration of the serum were varied with different individuals. The clinical course of the disease showed no remarkable change following this form of therapy according to the opinions of these physicians and the physicians and nurses who were in charge of the six patients.

Five of the most severely infected children were given the nonspecific immunotransfusion therapy as outlined by Crocker, Valentine and Brody[1] in the Philadelphia General Hospital in 1932. The splendid results from the use of this therapy during the past three years in the treatment of septicemia, pneumonia[2-6] and other acute infections gave promise of equally good or more effective results in the treatment of typhoid fever.

The patients treated with nonspecific immunotransfusions were selected because of their high temperature, marked toxicity and wide left shift in the Schilling hemogram. All patients except R. D. (Case 4), who had a relapse, were quite toxic at the time of transfusion. Three of these were treated in the second week of the disease and three in the

first few days of a relapse. All five patients had had positive blood cultures, and two of these had been positive within five days of receiving the transfusions. Following this treatment all patients showed immediate marked improvement as detailed in the case reports.

Modified Schilling hemograms[7] were used to control the therapy. An extensive left shift in the hemogram twenty-four or more hours after treatment indicated that further transfusions were needed, and a right shift after treatment indicated that no additional transfusions were necessary. Shiftograms or charts of sequential hemograms were used to follow the course of the disease. The vertical graph, or shiftograph on the shiftograms, is a graphic representation of the successive Schilling indices, and shows at a glance the shift to the right or left from day to day, as the process improves or retrogresses during the entire course of the disease.

### PREPARATION OF THE DONOR

A suitable donor is selected according to general health, serology, typing, and cross agglutination. He is hospitalized and fifty million killed typhoid bacilli are given intravenously. The usual stock typhoid or mixed typhoid, paratyphoid A and B vaccine, one billion organisms per cubic centimeter, is used, of which $\frac{1}{20}$ c.c. is the dose. If the donor does not have a reaction within an hour, the dose is repeated. Usually within an hour after injection of the killed organisms, the donor has a chill followed by a rise in temperature to from 102 to 104° F. and leucocytosis up to 25,000. This reaction continues for an hour or more, but the temperature returns to normal within a few hours. Eight hours after the injection of typhoid vaccine the donor's blood is taken. It is given to the patient by the direct or indirect method in two transfusions of from 100 to 200 c.c. on two successive days. Five hundred cubic centimeters of blood are drawn from the donor and that which is not used in the first transfusion may be kept safely in the ice box for seventy-two hours.

### RATIONALE OF THE TREATMENT

The fifty million killed typhoid organisms are given to the donor intravenously as a standard, safe and effective dose of foreign protein for the purpose of producing in him a foreign protein reaction. They stimulate the donor's cells to a maximum production of opsonins, or nonspecific immune bodies, in approximately eight hours. Crocker, Valentine, and Brody have shown that the opsonins are increased in this manner from fivefold to tenfold. The opsonins, or nonspecific immune bodies, are transferred from the donor to the patient as a form of passive immunity where they so affect the bacteria in the patient that his leucocytes may readily phagocytize them and thus reduce the intoxication.

The typhoid vaccine is not given to the donor with the idea of stimulating his cells to the production of specific antibodies against the typhoid bacilli, as precipitins, agglutinations or lysins, in a period of eight hours. This does not occur. All Widal reactions on the donor's serum eight hours after injection of the vaccine intravenously were negative for typhoid bacillus agglutinins. For this reason it is assumed that the other specific immune bodies, precipitins and lysins, are also absent, but further work along these lines is planned. On the basis of negative Widal reactions for specific typhoid agglutinins and a positive increase of opsonins or nonspecific immune bodies on the donor's blood eight hours after intravenous injection of fifty million killed typhoid organisms, this method is considered to be a nonspecific immunotransfusion therapy.

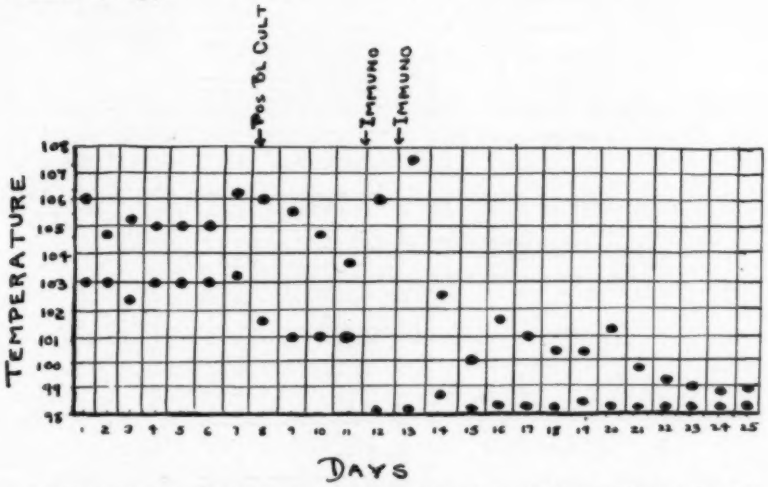


Chart 1.—Case 1. Markedly severe primary infection. Marked reaction after each of two nonspecific immunotransfusions with immediate improvement and subsequent recovery. In this and subsequent clinical charts the two readings for each day represent the highest and lowest temperatures during that day. *Immuno* indicates nonspecific immunotransfusion.

## CASE REPORTS*

CASE 1.—A. B., a negro female, aged three years, was admitted July 12, 1935, with fever of two days' duration, vomiting, and loss of weight. Exposure was not known, and the onset was uncertain. She was very toxic with throat markedly inflamed, typical appearance of tongue, coarse râles throughout the chest and distention of abdomen. On July 13 the red blood cells were 4,340,000, white blood cells, 5,550; polymorphonuclears, 64 per cent; lymphocytes, 30 per cent; monocytes, 6 per cent. On July 15 rose spots developed; the Widal reaction was positive 1:640; and the blood culture was positive for typhoid. Treatment was symptomatic, and the patient continued to be very fretful, toxic, with a temperature of 103 to 106° F., abdomen markedly distended, and occasional vomiting and diarrhea. On July 23, the twelfth day of illness, with a multiple index of 104 in the Schilling

*These patients were admitted to the pediatric service of Wm. N. Bradley, M.D.

| Date 1926 | Day of illness | Pos. blood culture | Bomp. Inm. Transf. | C.G. of blood | Grams hemoglobin | Red blood cells | White blood cells | Multiple index degrees of toxicity | Sedilling index | Myelocytes | Juvenalles | Stabs | Segmenters | Total neutrophiles | Lymphoblasts | Large lymphs | Intermediate lymphs | Small lymphs | Total lymphs | Monocytes | Eosinophiles | Basophiles | Segmenters cmm | Total neutrophiles cmm | Total lymphs cmm | Monocytes cmm |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Day | C | Tr | c.c. | Hb 15.4 | RBC 5.0 | WBC 7500 | MI 1 | ShI 1/16 | M 0 | J 0 | St 4 | Sg 64 | TH 68 | Lb 0 | L 5 | I 20 | S 20 | TL 25 | M 4 | E 2 | B 0 | Sg 4800 | TH 5000 | TL 2000 | M 300 Normals |
| | | | | | | | | | | | | | | | | | | | | | | | | | |
| 7-15 | 4 | + | | | 14.0 | 4.3 | 9400 | 59 | 3.1 | 0 | 0 | 60 | 16 | 76 | 0 | 6 | 0 | 4 | 10 | 14 | 0 | 0 | 1504 | 7144 | 940 | 1316 |
| 7-22 | 11 | | | | 13.0 | 3.8 | 6450 | 176 | 1.5 | 0 | 0 | 44 | 4 | 48 | 2 | 4 | 0 | 40 | 46 | 6 | 0 | 0 | 248 | 2975 | 2941 | 384 |
| 7-23 | 12 | | 1 | 90 | 13.0 | 3.7 | 6700 | 104 | 6.5 | 0 | 0 | 32 | 8 | 40 | 2 | 10 | 0 | 10 | 20 | 18 | 2 | 0 | 536 | 4020 | 1340 | 1206 |
| 7-24 | 13 | | 2 | 100 | 13.0 | 3.6 | 7200 | 24 | 1.5 | 0 | 0 | 28 | 18 | 46 | 0 | 16 | 0 | 22 | 48 | 16 | 0 | 0 | 1296 | 3312 | 3466 | 432 |
| 7-25 | 14 | | | | 13.0 | 3.4 | 8750 | 52 | 3.3 | 0 | 0 | 34 | 16 | 70 | 0 | 10 | 0 | 8 | 18 | 12 | 0 | 0 | 1752 | 6090 | 1576 | 1044 |
| 7-26 | 15 | | | | 12.0 | 3.2 | 7150 | 64 | 4.0 | 0 | 0 | 40 | 10 | 50 | 0 | 20 | 0 | 20 | 40 | 10 | 0 | 0 | 710 | 3550 | 2840 | 710 |
| 7-27 | 16 | | | | 12.0 | 3.2 | 5600 | 36 | 2.3 | 0 | 0 | 28 | 16 | 54 | 0 | 2 | 0 | 34 | 36 | 10 | 0 | 0 | 896 | 3024 | 2016 | 560 |
| 7-29 | 18 | | | | 13.0 | 3.6 | 7700 | 24 | 1.5 | 0 | 0 | 22 | 18 | 46 | 0 | 26 | 0 | 12 | 38 | 16 | 0 | 0 | 1386 | 3542 | 2926 | 1232 |
| 8- 2 | 22 | | | | 13.0 | 4.0 | 8100 | 17 | 1.1 | 0 | 0 | 22 | 20 | 42 | 0 | 4 | 0 | 48 | 52 | 6 | 0 | 0 | 1620 | 3402 | 4212 | 486 |
| 8- 8 | 28 | | | | 14.0 | 4.2 | 7900 | 9 | 3/5 | 0 | 0 | 12 | 20 | 32 | 0 | 6 | 0 | 58 | 64 | 4 | 0 | 0 | 1580 | 2528 | 5056 | 316 |
| 8-14 | 34 | | | | 14.0 | 4.2 | 7000 | 13 | 6/7 | 0 | 0 | 18 | 22 | 40 | 0 | 10 | 0 | 46 | 56 | 8 | 2 | 0 | 1540 | 2800 | 3920 | 112 |
| 8-16 | 36 | | | | 14.0 | 4.3 | 10500 | 12 | 4/5 | 0 | 0 | 8 | 10 | 18 | 0 | 12 | 0 | 64 | 76 | 2 | 4 | 0 | 1050 | 1890 | 7980 | 210 |

Chart 2.—Case 1., A. B. Shiftogram of a case of typhoid fever illustrating wide alternating shifts to the left and right during the first twelve days of illness. On the twelfth day the first nonspecific immunotransfusion of 90 c.c. was given, which forced the shift to the right from a Schilling index of 6.5 to 1.5 or a multiple index of 104 to 24 or reduced the toxicity of the patient from 104 to 24 degrees in twenty-four hours. The second nonspecific immunotransfusion of 100 c.c. was given on the thirteenth day to reinforce the first. During the following forty-eight hours, the reaction between the opsonins of the nonspecific immunotransfusion and the toxins of the bacteria was in doubt, the shift extending to the left to a Schilling index of 4 and a multiple index of 64. On the fifteenth day the opsonins overcame the bacteria, and the shift was forced to the right to convalescence and recovery.

hemogram, the first nonspecific immunotransfusion of 90 c.c. was given. The patient had a chill, and the temperature rose to 106° F. The next day the second treatment was given and was followed by a chill and an elevation of temperature to 107.5° F. Improvement occurred quickly. Within twenty-four hours the multiple index dropped from 104 to 24 (normal multiple index, 1). The temperature dropped to normal within forty-eight hours, rising to 101° F. only twice during the next few days. The toxicity was greatly lessened, and in three days the abdominal distention had disappeared. Improvement continued until August 6, when the urine and the feces were negative for typhoid bacilli. The patient was discharged Aug. 22, 1935. This was the only patient not definitely associated with the epidemic of June, 1935.

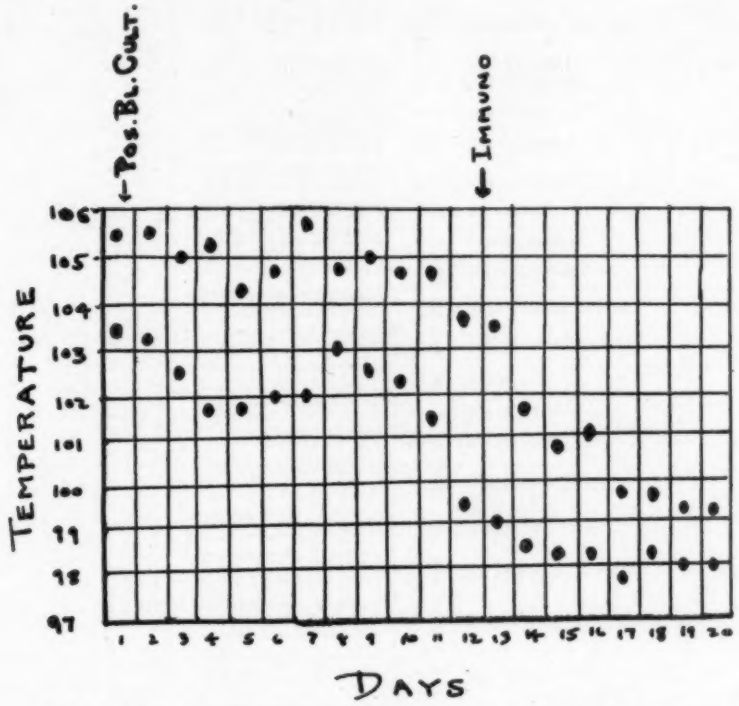


Chart 3.—Case 2. Moderately toxic primary infection with intestinal hemorrhage. One nonspecific immunotransfusion was followed by drop in temperature and recovery.

Case 2.—T. H., white female, aged eight years, was exposed May 30, 1935; the onset was on June 19, with fever, dizziness, and anorexia. She was admitted June 24, in a toxic condition with rose spots, typical appearance of the tongue, nontransmitted apical systolic murmur, palpable spleen, and slight distention. On June 24 the red blood cells were 4,500,000 per cubic millimeter, white blood cells, 4,900; neutrophiles, 58 per cent; lymphocytes, 42 per cent; and the blood culture was positive for typhoid organisms. On June 27 the stools were bloody; the child was toxic and drowsy and was taking nourishment poorly, was vomiting frequently, and had slight abdominal distention. Temperature ranged between 103 and 105° F., becoming septic in type on July 5. One nonspecific immunotransfusion of 150 c.c. was

Chart 4.—Case 2., T. H. Shiftogram of a case of typhoid fever illustrating a right shift to convalescence and recovery following one nonspecific immunotransfusion of 150 c.c. given July 6, 1935, on the thirteenth day of illness. Twenty-four hours after the transfusion the multiple index or degrees of toxicity dropped from 304 to 48, and the Schilling index, from 19 to 3. Slight alternating shifts to the left and right continued within convalescent limits to recovery. The shiftograph is a vertical graphic representation of the successive Schilling indices and shows the shift to the left or right at a glance.

given July 6, the thirteenth day of illness. No definite reaction followed, but the temperature became normal in four days with improvement in appetite and alertness and with disappearance of diarrhea and distention. At the same time the hemogram showed a shift to the right from a multiple index of 304 to 48 within forty-eight hours. The urine and the feces were negative July 19, and the patient was discharged Aug. 9, 1935.

Case 3.—V. A., white male, aged nine years, was exposed May 30, 1935; the onset was on June 16 with malaise, fever, anorexia, and diarrhea. He was admitted June 23 in a toxic condition, with rose spots, typical appearance of the tongue, bronchitis, dicrotic pulse, slight abdominal distention, palpable spleen, and moderate deafness in both ears. On June 23 the red blood cells numbered 5,100,000; white blood cells, 8,900; neutrophiles, 76 per cent; lymphocytes, 18 per cent; monocytes, 6 per cent. On June 24 the blood culture was positive for typhoid organisms, and the Widal reaction was positive 1:20. With symptomatic treatment the temperature ranged

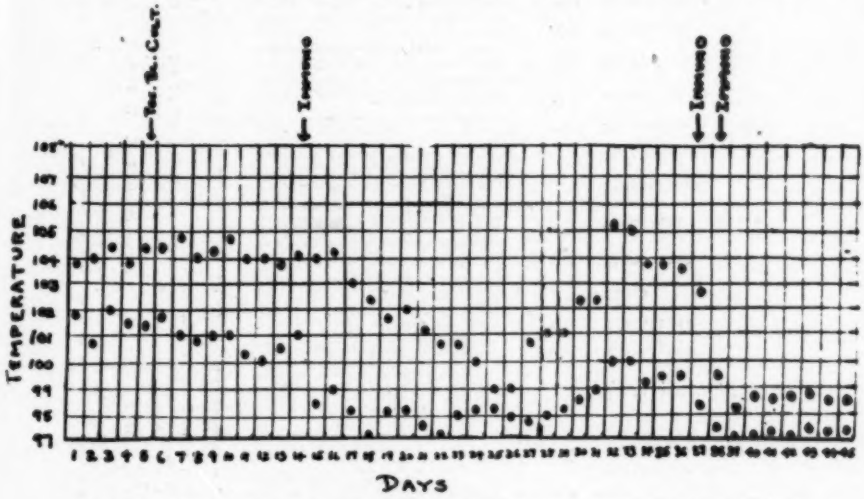


Chart 5.—Case 3. Severely toxic primary infection. One nonspecific immunotransfusion induced prompt symptomatic improvement but more gradual temperature drop. Recurrence followed by recovery after two additional nonspecific immunotransfusions.

from 101 to 105° F.; the patient was very toxic and irritable, had marked anorexia and moderate distention, and showed no signs of improvement. On the fourteenth day of illness, July 6, when the multiple index was 192, the first nonspecific immunotransfusion of 150 c.c. was given. There was no reaction, but the multiple index decreased to 32 within twenty-four hours, and the temperature became irregular and gradually defervesced to normal in nine days. The patient sat up and was no longer toxic or lethargic; his hearing was improved. This convalescence continued for approximately ten days when on the twenty-fourth day of illness, July 16, a relapse began. The temperature rose to 104° F. on July 27, with return of his previous toxicity and lethargy and a left shift in the hemogram from a multiple index of 12 to 128. On July 28 the second nonspecific immunotransfusion of 150 c.c. was given, followed by the third of 140 c.c. the next day. The temperature became normal in twenty-four hours, and the multiple index of the hemogram fell from 102 to 16. The urine and the feces were negative for typhoid organisms on August 6, and the patient was discharged Aug. 19, 1935.

| Date 1935 | Day of illness | Pos. blood culture | Hemop. Inm. Transf. | C.C. of blood | Grams hemoglobin | Red blood cells | White blood cells | Multiple index Degrees of toxicity | Schilling Index | Myelocytes | Juveniles | Stabs | Segmenters | Total neutrophiles | Lymphoblast | Large lymphs | Intermediate lymphs | Small lymphs | Total lymphs | Monocytes | Eosinophiles | Basophiles | Segmenters cmm | Total neutrophiles cmm | Total lymphs cmm | Monocytes cmm |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 24hr | 21 | 18 | 15 | 12 | 9 | 6 | 3 | 1 C.C. | | | | | | | | | | | | | | |
| 6-24 | 21 | + | | | 15 | 5.1 | 9900 | 155 | 7.7 | 0 | 0 | 78 | 8 | 86 | 2 | 2 | 0 | 10 | 14 | 0 | 0 | 0 | 712 | 7654 | 1246 | 000 |
| 6-29 | 7 | | | | 10 | 3.1 | 6000 | 209 | 13.0 | 0 | 0 | 80 | 6 | 86 | 4 | 2 | 2 | 6 | 14 | 0 | 0 | 0 | 516 | 5160 | 840 | 000 |
| 7- 5 | 13 | | | | 10 | 3.2 | 4200 | 48 | 1.2 | 0 | 0 | 60 | 20 | 80 | 4 | 0 | 0 | 12 | 20 | 0 | 0 | 0 | 840 | 3360 | 840 | 000 |
| 7- 6 | 14 | | | 1150 | 10 | 3.0 | 4500 | 192 | 12.0 | 0 | 0 | 72 | 6 | 78 | 0 | 0 | 0 | 16 | 22 | 0 | 0 | 0 | 270 | 3510 | 990 | 000 |
| 7- 7 | 15 | | | | 10 | 3.0 | 4300 | 32 | 2.0 | 0 | 0 | 40 | 20 | 60 | 0 | 0 | 0 | 18 | 30 | 8 | 2 | 0 | 860 | 2580 | 1230 | 344 |
| 7- 9 | 17 | | | | 10 | 3.0 | 4300 | 19 | 1.2 | 0 | 0 | 26 | 32 | 50 | 0 | 0 | 0 | 28 | 32 | 16 | 2 | 0 | 946 | 2150 | 1376 | 688 |
| 7-11 | 19 | | | | 12 | 3.4 | 3900 | 80 | 1.5 | 0 | 0 | 24 | 26 | 50 | 4 | 4 | 0 | 24 | 32 | 8 | 3 | 0 | 1014 | 2340 | 1248 | 312 |
| 7-18 | 26 | | | | 12 | 3.6 | 5000 | 12 | 3/4 | 0 | 0 | 24 | 40 | 64 | 16 | 2 | 2 | 6 | 24 | 2 | 0 | 0 | 2000 | 3700 | 1200 | 100 |
| 7-22 | 30 | | | | 13 | 4.3 | 8000 | 35 | 2.2 | 0 | 0 | 36 | 16 | 52 | 10 | 0 | 2 | 14 | 24 | 24 | 0 | 0 | 1280 | 4160 | 1920 | 1920 |
| 7-24 | 32 | | | | 13 | 4.3 | 7600 | 129 | 8.0 | 0 | 0 | 64 | 8 | 72 | 0 | 6 | 2 | 8 | 16 | 12 | 0 | 0 | 608 | 5472 | 1216 | 912 |
| 7-28 | 36 | | | 2150 | 13 | 4.2 | 8200 | 102 | 6.4 | 0 | 0 | 44 | 10 | 74 | 0 | 6 | 0 | 2 | 8 | 8 | 0 | 0 | 820 | 6068 | 1476 | 656 |
| 7-29 | 37 | | | 3150 | 13 | 4.4 | 11200 | 16 | 1.0 | 0 | 0 | 32 | 34 | 66 | 0 | 6 | 0 | 2 | 8 | 26 | 0 | 0 | 3808 | 7392 | 896 | 2912 |
| 8- 2 | 41 | | | | 13 | 4.3 | 10200 | 30 | 1.9 | 0 | 0 | 30 | 20 | 50 | 0 | 18 | 0 | 8 | 26 | 14 | 2 | 0 | 2040 | 5916 | 2652 | 1428 |
| 8- 4 | 43 | | | | 13 | 4.4 | 10400 | 14 | 7/8 | 0 | 0 | 30 | 34 | 64 | 0 | 8 | 2 | 24 | 34 | 1 | 1 | 0 | 3536 | 6656 | 3536 | 104 |
| 8- 8 | 47 | | | | 13 | 4.3 | 11300 | 24 | 1.5 | 0 | 0 | 36 | 22 | 58 | 0 | 12 | 0 | 28 | 40 | 0 | 2 | 0 | 2486 | 6554 | 4520 | 000 |
| 8-14 | 53 | | | | 13 | 4.4 | 9700 | 8 | 1/2 | 0 | 0 | 20 | 46 | 66 | 0 | 4 | 0 | 22 | 26 | 6 | 2 | 0 | 4462 | 6402 | 2522 | 582 |
| 8-16 | 55 | | | | 13 | 4.5 | 8400 | 10 | 2/3 | 0 | 2 | 24 | 36 | 62 | 0 | 10 | 0 | 20 | 30 | 4 | 2 | 2 | 3024 | 5208 | 2520 | 336 |
| | | | | | | | | | | | | | | | | | | | | | | Normals | | | | 300 |

Chart 6.—Case 3., V. A. Shiftogram of a case of typhoid fever illustrating wide alternating shifts to the left and right during the first thirteen days of illness. On the fourteenth day the first nonspecific immunotransfusion of 150 c.c. forced the shift right from a Schilling index of 12 to 2 and from a multiple index of 192 to 32, or reduced the toxicity from 192 to 32 degrees. The shift remained right for a period of eleven days, reaching the low multiple index of 13 on the twenty-sixth day of illness. On the twenty-sixth day a relapse began. The toxin forced the shift left during the next six days, reaching a Schilling index of 8 and a multiple index of 128 by the thirty-second day. The second nonspecific immunotransfusion was given four days later on the thirty-sixth day of illness, when the Schilling index was 6.4 and the multiple index 102. It forced the shift right in twenty-four hours to a Schilling index of 1 and a multiple index of 16, or reduced the toxicity of the patient from 102 to 16 degrees. The third nonspecific immunotransfusion was given the following day, the thirty-seventh day of illness, to reinforce the second. Together these treatments kept the shift right within convalescent limits and by overcoming the infection brought about recovery.

CASE 4.—R. D., white female, aged nine years, was exposed May 30, 1935. The onset was on June 10, with stiff neck, fever, headache, abdominal pain, and cough. She was admitted on June 22, with rose spots and typical appearance of tongue. On June 22 the red blood cells numbered 4,440,000; white blood cells, 10,200; neutrophiles, 54 per cent; lymphocytes, 42 per cent; and monocytes, 4 per cent. On June 24 the blood culture was positive for typhoid bacilli, and the Widal reaction was positive 1:320. With symptomatic treatment the temperature varied from 102 to 105.5° F., and there was moderate toxicity and abdominal distention. By July 4 the temperature became normal; the hemogramic shift went to the right to a multiple index of 8, and the patient was clinically well, remaining so for a week. On July 16 the temperature again rose, and the hemogramic shift started left in a relapse with a return of toxicity, drowsiness, and anorexia. By July 22 the temperature was 105° F.; the multiple index, 96; and the blood culture was again positive. The first nonspecific immunotransfusion of 150 c.c. was given on July 26 and was followed by

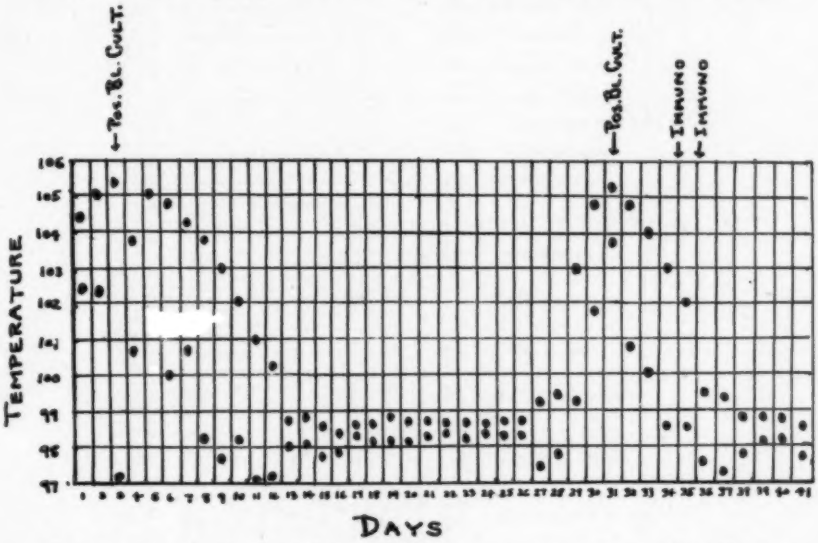


Chart 7.—Case 4. Moderately toxic patient in recurrence. Two nonspecific immunotransfusions followed by recovery.

a slight chill and a drop of the multiple index from 80 to 27 within twenty-four hours. The second nonspecific immunotransfusion of 150 c.c. was given the following day and caused a further drop in the multiple index from 27 to 16. Within the next twenty-four hours the temperature became normal; the signs of toxicity had disappeared; and the patient was clinically well. The urine and the feces were negative for typhoid bacilli on August 6, and the patient was discharged Aug. 17, 1935.

CASE 5.—J. F., white male, aged ten years, was exposed May 30, 1935; the onset was on June 15 with malaise, headache, anorexia, and epistaxis. He was admitted June 22 with tongue typical, spleen palpable and abdominal distention slight. On June 22 red blood cells numbered 5,140,000; white blood cells, 10,700; neutrophiles, 74 per cent; lymphocytes, 22 per cent, and monocytes, 4 per cent. The blood culture was positive for typhoid bacilli, and the Widal reaction was positive 1:80 on June 24. The patient rapidly became worse, the temperature remaining from 103 to 106° F.: he was very toxic and stuporous. Intravenous glucose and saline were used for sev-

| Date 1925 | Day of illness | Day C | Tr | o.c. | Pos. blood culture | Homog. Ime. Treatm. | C.C. of blood | Grams hemoglobin | Red blood cells | White blood cells | Multiple index degrees of toxicity | Sedilling index | Myelocytes | Juveniles | Stabs | Segmenters | Total neutrophiles | Lymphoblasts | Large lymphs | Intermediate lymphs | Small lymphs | Total lymphs | Monocytes | Eosinophiles | Basophiles | Segmenters cmm | Total neutrophiles cmm | Total lymphs cmm | Monocytes cmm | Normals |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Hb | RBC | WBC | MI | Shi | M | J | St | Sg | Th | Lb | L | I | S | TL | M | E | B | Sg | TN | TL | M | |
| | | | | | | | | 15.4 | 5.0 | 7500 | 1 | 1/16 | 0 | 0 | 4 | 64 | 68 | 0 | 5 | 1 | 20 | 26 | 4 | 2 | 0 | 4800 | 5000 | 2000 | 300 | |
| 6-24 | 3 | | | | | | | 14.0 | 4.4 | 10200 | 78 | 4.0 | 0 | 0 | 52 | 12 | 64 | 2 | 0 | 0 | 24 | 26 | 8 | 0 | 0 | 1224 | 6732 | 2652 | 816 | |
| 6-29 | 8 | | | | | | | 14.0 | 4.5 | 8200 | 54 | 4.0 | 0 | 0 | 48 | 12 | 60 | 4 | 12 | 4 | 16 | 36 | 4 | 0 | 0 | 984 | 4920 | 2952 | 328 | |
| 7- 2 | 11 | | | | | | | 14.0 | 4.4 | 8600 | 35 | 2.1 | 0 | 0 | 28 | 12 | 40 | 2 | 14 | 0 | 26 | 42 | 20 | 0 | 0 | 1036 | 3268 | 3612 | 1720 | |
| 7- 4 | 13 | | | | | | | 14.0 | 4.3 | 7600 | 8 | 1/2 | 0 | 0 | 20 | 40 | 60 | 2 | 6 | 0 | 30 | 38 | 4 | 0 | 0 | 3040 | 4560 | 2736 | 304 | |
| 7-10 | 20 | + | | | | | | 14.0 | 4.2 | 7400 | 6 | 1/2 | 0 | 0 | 16 | 48 | 64 | 0 | 2 | 2 | 26 | 32 | 4 | 0 | 0 | 3552 | 4736 | 2368 | 296 | |
| 7-16 | 26 | | | | | | | 13.0 | 3.8 | 7100 | 6 | 2/3 | 0 | 0 | 30 | 50 | 70 | 0 | 4 | 2 | 24 | 26 | 4 | 0 | 0 | 3550 | 4970 | 1846 | 284 | |
| 7-22 | 32 | | | | | | | 13.0 | 3.8 | 8000 | 80 | 5.0 | 0 | 0 | 50 | 10 | 60 | 4 | 8 | 2 | 20 | 30 | 10 | 0 | 0 | 800 | 4800 | 2400 | 800 | |
| 7-25 | 35 | | | | | | | 13.0 | 3.7 | 7200 | 96 | 6.0 | 0 | 0 | 36 | 6 | 42 | 4 | 8 | 2 | 36 | 50 | 6 | 0 | 0 | 432 | 3024 | 3600 | 576 | |
| 7-26 | 36 | | | 150 | | | | 13.0 | 3.7 | 10100 | 80 | 5.0 | 0 | 0 | 10 | 8 | 48 | 0 | 2 | 0 | 50 | 52 | 0 | 0 | 0 | 808 | 4848 | 5252 | 000 | |
| 7-27 | 37 | | | 150 | | | | 13.0 | 3.6 | 6100 | 27 | 1.7 | 0 | 0 | 22 | 14 | 36 | 0 | 2 | 0 | 54 | 56 | 4 | 0 | 0 | 864 | 2318 | 3536 | 244 | |
| 7-28 | 38 | | | | | | | 13.0 | 3.8 | 10300 | 16 | 1.0 | 0 | 0 | 16 | 16 | 32 | 0 | 2 | 0 | 56 | 58 | 6 | 0 | 0 | 1648 | 3296 | 5974 | 618 | |
| 7-31 | 41 | | | | | | | 13.0 | 3.7 | 11800 | 17 | 1.1 | 0 | 0 | 13 | 15 | 28 | 2 | 46 | 0 | 16 | 64 | 2 | 0 | 0 | 1888 | 4012 | 7552 | 236 | |
| 8- 2 | 43 | | | | | | | 13.0 | 3.8 | 10600 | 12 | 3/4 | 0 | 0 | 18 | 22 | 40 | 0 | 2 | 0 | 40 | 42 | 18 | 0 | 0 | 2332 | 4240 | 4452 | 1908 | |
| 8-14 | 55 | | | | | | | 14.0 | 4.2 | 10000 | 16 | 1.0 | 0 | 0 | 20 | 20 | 40 | 0 | 12 | 0 | 42 | 54 | 4 | 2 | 0 | 2000 | 4000 | 5400 | 400 | |

Chart 8.—Case 4., R. D. Shiftogram of a patient with typhoid fever, illustrating a spontaneous right shift to convalescence after the first week of illness; a wide left shift indicating a relapse on the thirty-second day; two nonspecific immunotransfusions of 150 c.c. each on the thirty-sixth and thirty-seventh days, followed by a right shift to convalescence and recovery.

eral days; then tube feeding was started and continued for fifty-three days. Between June 25 and July 12 he received nine intramuscular injections of human specific immune serum, which produced no clinical improvement. Two ordinary blood transfusions had also been given with no effect on the clinical condition. On July 12 the

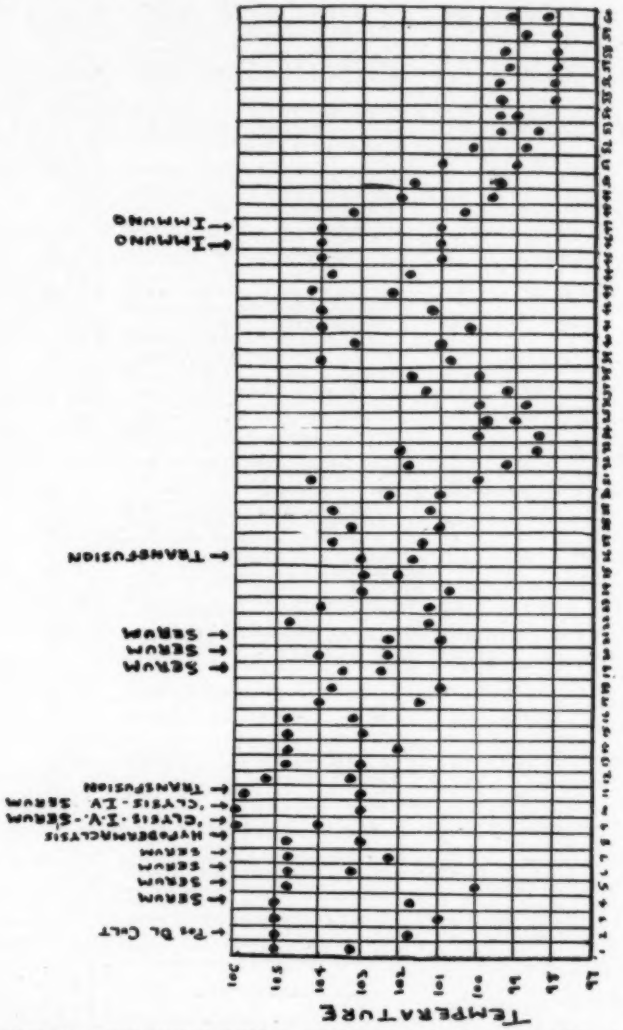


Chart 9.—Case 5. Severely toxic primary infection with temporary improvement followed by equally severe recurrence of symptoms. No response to various types of treatment until nonspecific immunotransfusions were given, which were followed by recovery. Transfusion refers to the ordinary type.

patient developed nuchal rigidity, positive Brudzinski reflex, ankle clonus, and bilateral positive Babinski reflex, but the spinal fluid cell count, smear, and culture were all negative. The hemogramic shift went left from 8 on July 12 to 70 on July 29. There was slight clinical improvement with a drop in temperature from July 21 until July 29, although he was still stuporous and required tube feeding. On July 29 the temperature rose to 104° F., and the multiple index to 70, with a return of the extremely toxic stuporous stage accompanied by marked diarrhea. On August 6 the

| Date 1935 | Day of illness | Pos. Blood culture | Hemp. Jm. Trans. | c.c. of blood | Grams hemoglobin | Red blood cells | White blood cells | Multiple index Degrees of toxicity | Schilling index | Myelocytes | Juveniles | Stabs | Segmenters | Total neutrophiles | Lymphoblasts | Large lymphs | Intermediate lymphs | Small lymphs | Total lymphs | Monocytes | Eosinophiles | Basophiles | Segmenters cmm | Total neutrophiles cmm | Total lymphs cmm | Monocytes cmm |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | | | | | | |

first nonspecific immunotransfusion was given with no definite reaction, and it was repeated the next day, a total of 385 c.c. being given. Following these treatments, the temperature began to fall and reached normal in three days. The multiple index of the hemogram dropped from 67 to 33. Improvement was marked; stupor decreased; diarrhea disappeared; he took some food by mouth and talked rationally. Convalescence was then uninterrupted. The urine and the feces were negative August 20, and the patient was discharged Sept. 11, 1935.

## DISCUSSION OF THE LITERATURE ON THE TREATMENT OF TYPHOID FEVER

The medical profession of this country for the past twenty-five years or more has been concerned with typhoid fever chiefly from the standpoint of its prevention. This work has been so successful that there have been but few epidemics large enough to offer opportunities for advancement in the treatment of the disease. The greatest improvement in typhoid fever therapy in this country was the introduction of the high caloric diet in place of the old time regimen of "starving the fever."

In Europe, on the other hand, there have been and still are fairly frequent epidemics, and in recent years much work has been done there in attempting to find a specific treatment for the disease. The following chemical and biological products have been used with varying degrees of success:

Drugs—neoarsphenamine, quinine bismuth iodide, alkalies, insulin, peptone intramuscularly, epinephrine, thymus extracts, sodium salicylate, amidopyrine, colloidal silver, strophanthin, barium chloride, atropine, sulphur, milk injections, salyrgan, methenamine, and mercurochrome.

Biologicals—antivirus, bacteriophage, Rodet's serum, autohemotherapy, typhoid vaccine (subcutaneous, intracutaneous, intravenous) antityphoid horse serum, and specific immunotransfusions.

The best results published on the treatment of typhoid fever have been with biologicals, especially with bacteriophage and specific immunotransfusions. The most extensive work with these methods has been done by the French clinicians. Bacteriophage was the earlier method. It was found to be of definite value by Manoussakis,[8] who reviewed work done by other Frenchmen with the same method. Its chief value was in carriers and in prolonged cases which were refractive to ordinary treatment.

More recent interest has been developed in the so-called specific immunotransfusions,* in which the donor has been a patient who has re-

*Our understanding of the types of transfusions to which we have referred is the following:

1. An ordinary transfusion is one in which the donor's blood is used in its natural state, with no special treatment of the donor before the transfusion. It may be given by the direct or indirect method.
2. A specific immunotransfusion[12] is one in which the donor has obtained a specific active immunity against the disease affecting the patient by having had and recovered from that disease or in which the donor is given an artificial active immunity by single or repeated subcutaneous or intramuscular injections of killed or attenuated organisms specific for the disease from which the patient is suffering.
3. A nonspecific immunotransfusion is one in which the donor is given an intravenous injection of some foreign protein which causes a maximum increase in opsonins or nonspecific immune bodies in his serum in approximately eight hours. Fifty million killed typhoid or mixed typhoid and paratyphoid A and B organisms is a standard, safe, and effective dose of foreign protein.

covered from typhoid fever or someone who has been vaccinated against the disease within the year preceding the time of the transfusion. The original work in this field was done by Tzanck,[9] who with Tremolieres published a detailed report of ten cases so treated. Their studies have been confirmed by DeSize,[10] Villaret, Justin-Besançon and Desoille,[11] Roueche,[12] and Eschbach.[13] This type of therapy was also used in prolonged cases and in those requiring transfusion because of marked intestinal hemorrhage.

Grassat[14] in South Africa has used a specially prepared concentrated horse serum intramuscularly in 130 cases of typhoid fever with a drop in temperature to normal within five or six days and with clinical improvement. Spiropoulos[15] reports the use of typhoid vaccine given intravenously in fifty cases of typhoid fever with a resultant drop in temperature and with no after-effects.

Typhoid vaccine has been used subcutaneously by Crough[16] in patients already infected, but his conclusions were that to get a decrease in duration and severity of the disease the three immunizing doses must be given before the onset of symptoms. This obviously limits its use to those patients definitely known to have been exposed. Daily doses of typhoid vaccine detoxicated with formalin and phenol were given by Wherry, LeBlanc, Foshay, and Thomas[17] early in the disease with shortening of the course but no immediate results.

## COMMENT

This series of patients has served the purpose of demonstrating the variability of the clinical picture of typhoid fever in children even when all extrinsic factors are similar, especially as regards the classical symptoms.

The diagnosis is easily established through laboratory methods after the disease is suggested by a history of prolonged fever with no other definite cause and the presence of a few characteristic physical signs. Those patients who showed only fever, malaise, and anorexia might not have been hospitalized or correctly diagnosed had not the parents been made "typhoid conscious" by the newspaper publicity given to the epidemic.

The mildness of the disease in the majority of these patients and their response to symptomatic medical treatment must not be misleading because typhoid fever in children can be a serious disease. Several children infected in this epidemic and admitted to other hospitals in the city died because of the overwhelming toxemia. Patient 5 is an example of the classical "typhoid state" occurring in a child.

It was the markedly toxic patients with continued high temperature, abdominal distention, apathy, stupor, and an alarming shift to the left in the Schilling hemogram to a multiple index close to 100 or above which induced us to seek a more effective form of therapy for this dis-

ease. The five patients receiving the nonspecific immunotransfusions ranged in toxicity from 2+ to 5+ and, clinically, included the sickest children on the ward. The charts clearly show the marked drop in temperature range and the extensive shift to the right in the hemograms after treatment in all five patients. Clinically, at the same time, their decrease in toxicity was shown by disappearance of lethargy, increase in appetite, lessening of diarrhea, and decrease of abdominal distention. Patient 3 suffered a relapse after a single nonspecific immunotransfusion but recovered quickly following two more similar treatments given on successive days.

The acutely ill patients responded as readily to this type of therapy whether treated in the early stages of the disease or after prolonged illness. Patients 1 and 4, who had had positive blood cultures a few days before receiving the nonspecific immunotransfusions, had the greatest reactions in the form of chill and elevation of temperature immediately after being given the blood, and they showed the most rapid improvement clinically. Usually patients do not have a temperature reaction following nonspecific immunotransfusions.

Ordinary blood transfusions have been used in the treatment of typhoid fever many times in the past but never with any apparent direct effect. There was not a sufficient number of severely infected patients in this series to afford controls in which ordinary transfusions might have been used. Patient 5, however, received two ordinary transfusions during the course of his illness, with no improvement, but convalesced quickly following two nonspecific immunotransfusions.

There were no deleterious effects noted in either the donor or patient during the use of this procedure, the elevated temperature reactions in the patient being easily controlled by tepid sponges.

Review of the literature on the treatment of typhoid fever revealed nothing which held great promise of immediate good results in the acute form of the disease or which could be prepared and given as quickly and conveniently, economically, and safely as nonspecific immunotransfusion therapy.

## SUMMARY

1. An epidemic of typhoid fever is reported.

2. Nineteen children simultaneously infected were treated for typhoid fever.

3. All patients received high caloric diet therapy.

4. Six patients were treated with intramuscular injections of specific immune human serum with no marked effect.

5. Five very ill patients were given nonspecific immunotransfusion therapy with immediate marked improvement followed by recovery, this being the first time this form of treatment has been employed in typhoid fever.

6. The literature on the treatment of typhoid fever is discussed.

## CONCLUSIONS

While this series of patients is too small to justify conclusions regarding the relative merits of the different forms of therapy employed it may, perhaps, suggest that the mild form of typhoid fever in children may be amenable to high caloric diet therapy, that specific immune human serum given intramuscularly may not be fairly judged on so few patients, and that nonspecific immunotransfusion therapy in typhoid fever in children deserves continued usage when opportunity occurs, as, we believe, it has given promise of being a very helpful form of treatment in this disease.

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# DYSENTERY BACILLEMIA

PHILLIP E. ROTHMAN, M.D.
LOS ANGELES, CALIF.

THE occurrence of a recent case of sepsis due to the dysentery bacillus has prompted this review of similar cases for the purpose of evaluating their clinical significance. For over a decade after the isolation of the dysentery bacillus, it was generally believed that the organism produced an infection strictly localized to the intestine and adjacent lymph glands. This opinion was originally stated by Shiga and reemphasized by Jochman as late as 1911. In the 1908 edition of Jordan's *General Bacteriology*[1] the following statement is made concerning the presence of the dysentery bacillus: "It is found at autopsy in the mesenteric glands, but, as a rule not in the spleen or other internal organs, nor does it occur in the blood or urine." In 1912 Darling and Bates[2] reported a case with a positive blood culture, and since then twelve additional cases have been recorded. Glynn[3] has pointed out that an analogous situation exists in the history of typhoid fever. He calls attention to Osler's statement in the first edition of his book in 1892 concerning the rarity of the typhoid bacillus in the blood. Subsequent investigations altered his opinion, and in the 1912 edition is the observation that the presence of the bacillus may be demonstrated in the blood of practically all cases. Undoubtedly more cases of dysentery sepsis have occurred than appear on record but not in sufficient number to make tenable this attempted analogy with typhoid fever.

The following case was observed at the Children's Hospital:

A white girl, aged two years, was admitted with a history of diarrhea of five days' duration. The past history contained no significant facts. The present illness began abruptly with fever and diarrhea. On the third day, blood appeared in the stools, which numbered six to eight a day. Her condition failed to improve, and on admission, two days later, she was moderately dehydrated and obviously ill. The history apparently justified a preliminary diagnosis of bacillary dysentery. It was noticed at this time that the cardiac pulsations were unusually forcible and the heart sounds increased in intensity. In the absence of evidence of organic heart disease, no special significance was attached to these findings. During the next two days, the temperature fluctuated between 101° and 106° F. Intravenous fluids and a blood transfusion were administered, and the usual dietary and hygienic measures were instituted. Although sepsis was not suspected, a blood culture was obtained on the day following admission, because the blood transfusion provided a favorable opportunity and because we were at a loss to explain the severity of the illness. The diarrhea was mild and no blood was observed in the stools. Two days after admission marked abdominal distention and facial edema were noted. The bladder was not distended although the nurses reported that no urine had been voided during the previous forty-eight hours. (Such reports are not always reliable as a child wearing diapers may void small quantities without detection.) The character of the radial pulse strongly suggested an elevation of blood pressure. The determi-

From the Children's Hospital.

nation first made at this time was 138 systolic over 70 diastolic. Attempts at catheterization were unsuccessful because of an anomalous opening of the urethra into the vagina. Because of this malformation, it was thought that additional abnormalities of the kidneys or urinary tract probably existed with a resulting terminal hypertension and renal failure. The patient became comatose a few hours preceding death on the eighth day of her illness.

*Laboratory Reports.*—Blood count (seventh day), hemoglobin, 38 per cent; red blood cells, 4,350,000; white blood cells, 30,800; polymorphonuclear cells, 92 per cent; lymphocytes, 3 per cent; monocytes, 4 per cent; premyelocytes, 1 per cent; neutrophiles contained toxic changes.

Nonprotein nitrogen (eighth day) was 55 mg. per 100 c.c.

Blood culture (seventh day) produced *B. dysenteriae* (Flexner). Growth was very slow and appeared after one week. Agglutination with a known antiserum was positive in a dilution of 1:640.

Culture from the large intestine at autopsy produced *B. dysenteriae* (Flexner). Agglutination in a dilution of 1:320 was secured only after transplants in veal infusion broth had been made for ten days.

*Autopsy Report* (Dr. C. M. Hyland).—The examination showed evidence of a generalized anasarca with small amounts of fluid in the peritoneal and pleural cavities. The large intestine showed prominent lymphoid follicles with edema and cellular infiltration of the mucosal stroma. In a few places the superficial portions of the mucosa had desquamated and the remaining mucosa beneath these areas gave evidence of early necrosis. No areas of marked ulceration were found. Strangely enough, similar changes were found in the small intestine and were slightly more prominent. The mesenteric lymph glands were enlarged. The kidney sections stained with hematoxylin and eosin showed swollen glomerular tufts with proliferation of the cells covering these tufts. The capillaries were engorged. Many of the convoluted tubules contained casts, and there was considerable destruction of the lining epithelium. No scar tissue was evident. Azan carmine stains showed in addition to the above lesions, a thickening of the basement membrane of the glomerular tufts. The picture was that of an acute nephritis involving principally the glomeruli. There were no abnormalities other than the anomalous opening of the urethra into the vagina. This apparently produced no obstruction to the flow of urine.

*Final Diagnosis.*—Bacillary dysentery, dysentery septicemia, acute nephritis with hypertension and renal failure.

Darling and Bates[2] described a patient observed in Panama. He was an adult negro, acutely ill with a temperature of 101° F., abdominal pain and a bloody diarrhea. There were marked tenderness over the colon and enlargement of the liver and spleen. The course was unusually severe and characterized by large hemorrhages from the bowel. The blood culture on the seventh day was positive for *B. dysenteriae* (Shiga), which was agglutinated in a dilution of 1:2,000. Death occurred on the tenth day of illness. Autopsy showed the usual diphtheritic inflammatory process from the rectum to the ileocecal valve with isolated gangrenous areas.

Kendall and Day[4] reported the case of a girl, aged five years, who was ill for three days with fever, obstinate vomiting, and bloody diarrhea. The illness was unusually severe and the patient markedly prostrated. The stool culture was positive for *B. dysenteriae* (Shiga). The

blood culture obtained two days before death revealed *B. dysenteriae* (Shiga), paratyphoid beta, Morgan bacillus, *B. alkaligines*, and streptococci.

De Sautelle's patient,[5] the youngest on record, was a three-week-old breast-fed infant, ill for two days with a temperature of 105° F. The grandmother was ill with typhoid fever in the same house, and for that reason a blood culture was taken. This was positive for the dysentery organism (type not stated). The temperature remained high, and a watery diarrhea developed. After one week, a severe convulsion occurred, and spinal puncture revealed bloody fluid which on culture was positive for the dysentery bacillus. Death occurred shortly after the convulsion.

Ghon and Roman[6] reported five cases of dysentery sepsis in soldiers aged twenty to twenty-six years. All cases resembled mild typhoid. Typical diarrhea with blood and mucus was not present. Enlargement of the spleen occurred in three cases and an eruption similar to typhoid in two cases. The blood culture was positive for the "Y" dysentery organism in all cases on the third or fourth day of the disease. In one patient the urine culture was positive for Shiga organism. In only one individual was the stool culture positive.

Fränkel[7] reported a patient who presented a clinical picture suggestive of a mild but protracted case of typhoid. The strain cultured from the patient's blood agglutinated with the "Y" dysentery test serum in a dilution of 1:16,000.

Ledingham and Penfold's patient[8] had fever of five weeks' duration during which time *B. paratyphosus A* was recovered from the blood stream. An exacerbation occurred at the end of this period and a subsequent blood culture produced *B. dysenteriae* (Shiga). The patient had previously suffered with attacks of diarrhea and was considered a dysentery carrier. They believed that the intestinal lesion produced by the paratyphoid infection more readily permitted the dysentery organism to invade the blood stream. Recovery followed after twenty-three days, and during this time there was no return of blood or mucus in the dejecta.

TenBroeck's case[9] was a male infant, ill for two days, with marked prostration and a temperature of 105° F. Typhoid was suspected, and a blood culture was taken. *B. dysenteriae* (Flexner) was obtained on two occasions. Later the stools became typical of dysentery although repeated cultures were negative. The patient eventually recovered after a long illness.

Brünauer's patient[10] was a twenty-eight-year-old man, ill with fever, diarrhea, vomiting, and abdominal pain. The spleen was enlarged and a "typhoidlike" eruption was present. Blood culture on the twelfth day was positive for the "Y" dysentery. The course simulated typhoid and at the end of a month he was fever free.

Boyd[11] observed a patient while serving with the Salonika Force during the World War. The illness was of four days' duration and characterized by vomiting and bloody diarrhea. Blood and stool cultures produced the Flexner "Y" organism. The patient was sent back to the base, and no additional history was obtained. There were no symptoms that differed from the ordinary case of bacillary dysentery.

Through the courtesy of Dr. Arthur Black, the reports of three unpublished cases from the Peiping Union Medical College have been forwarded to me. The first case occurred in a Chinese male infant, aged one year, who was admitted with a history of a bloody diarrhea of four days' duration. The frequency of the bowel movements had progressively increased and amounted to about forty in a twenty-four-hour period. He was critically ill and markedly dehydrated. The temperature fluctuated between 39 and 40.4° C. The blood count on admission showed 5,540,000 red cells; hemoglobin, 14 gm., white blood cells, 30,450, with 80 per cent polymorphonuclear cells. Twelve hours before death the leucocytes numbered 45,500. One stool culture on the day of admission produced the Shiga organism. A blood culture obtained directly from the heart immediately postmortem also produced the Shiga organism.

The other two cases occurred in adults, and the records for a detailed report were not obtained from the general medical service. One patient was a Chinese male, aged thirty-two years, who died three days after an operation for an acute appendicitis. Blood culture, a day before death, produced *B. dysenteriae* of the mannite-fermenting group. The other case was a Chinese female, aged thirty-one years, admitted because of symptoms of sepsis following an induced abortion. Blood culture produced *B. dysenteriae* of the mannite-fermenting group. The patient recovered.

The following sentence from Dr. Black's communication is of interest: "In view of the fact that the number of cases of bacillary dysentery admitted to the hospital every year on all services ranges around three to four hundred with many times that number seen in the out-patient department, and, since the hospital has been open since 1922 with only these three cases, it is certainly clear that dysentery bacteremias are not common."

## DISCUSSION

The similarity to mild typhoid of nine of the thirteen cases previously reported deserves comment. Several of these patients had splenic enlargement and a typhoidlike eruption. Severe diarrhea with blood and mucus was rarely present. The temperature curve and duration of illness were consistent with typhoid fever. The resemblance has led several authors to state that this clinical picture is characteristic of dysentery sepsis. A more plausible explanation suggested by Ledingham and Penfold is the possibility of a mixed infection. Their case was one due to *B. parathyphosus A* followed by an acute exacerbation due to the

Shiga organism. Some of the cases mentioned herein reported by European writers occurred in soldiers during the World War, and statistics collected by Wolko[12] in 1915 indicate the frequent occurrence of mixed typhoid and dysentery infections in the German and Austrian reserve hospitals. Unfortunately this very satisfactory explanation lacks complete serologic confirmation. The cases reported by Boyd, Kendall and Day, Darling and Bates, and the case of the infant described by Dr. Black conform to the usual picture of severe dysentery. DeSautelle's case is the only one that clinically suggests sepsis. Despite the paucity of clinical data in some of the above reports, it is permissible to conclude that the presence of the dysentery organism in the circulating blood fails to produce any characteristic signs or symptoms that would enable one to arrive at even a tentative diagnosis without the necessity of laboratory aid. Of the seventeen cases now on record, including my own, there were six deaths. The series is too small to be certain that the presence of sepsis increases the mortality. In regard to this point it is of interest that in the records of the Children's Hospital, the most fulminating type of dysentery, in which death occurs within twenty-four or forty-eight hours after the onset, has not been accompanied by sepsis. The presence of sepsis does apparently favor the occurrence of complications. This is evident in Elsworthy's case[13] of postdysentery arthritis. De Sautelle's case with meningeal involvement, Gunn's case[14] of pneumonia in which the dysentery organism was isolated, Brünauer's case with a thrombophlebitis of the left crural vein, and my case with an acute nephritis.

The relatively insignificant necropsy findings in some of the cases with sepsis has been discussed by several authors. The origin of the intestinal lesions, as proved many years ago by Flexner and Sweet,[15] is due to the act of elimination of the toxin by the intestinal mucosa and not by the direct effect of the bacteria upon the surface of the mucous membrane. Their experiments on the comparative toxicity of living, dead, and autolysed cultures showed that the separated toxin is more effective than the same quantity of poison contained within the living or dead bacilli. The presence of living organisms in the blood is in itself of only secondary significance in the production of intestinal lesions. The latter depend on the amount of liberated toxin and its excretion by successive acts of elimination through the intestinal wall.

There is on record a considerable amount of evidence to support the contention that the dysentery organism invades the blood stream more frequently than is ordinarily believed. Many observers have obtained pure cultures of the bacteria from the heart's blood, spleen, liver, or bile at autopsy in patients who died with bacillary dysentery. Instances of this nature are enumerated in the article by Ghon and Roman and also in the review by Davison.[16] Typical examples are contained in the reports of Gunn,[14] Caussade and Marbais,[17] Rosenthal,[18] and Baerthlein and Huwald.[19] These cases are subject to criticism as postmortem

blood cultures are notoriously unreliable. Nevertheless, Gunn states definitely, "It is customary to accept a positive postmortem spleen culture, even in the case of motile bacteria, as evidence that a bacteremia had existed during life."

Positive cultures during life from the urine of male patients represent presumptive evidence of an existing bacteremia if one can exclude the possibility of contamination through feces. Brünauer has reported four cases, one of which occurred during convalescence from typhoid and another during a coexisting dysentery and paratyphoid infection. Fränkel observed one case in a series of thirty-six routine urine cultures.

The organism has been cultured from the joint fluid in a case of post-dysentery arthritis by Elsworthy. In a somewhat similar case, Clifford[20] found dysentery agglutinins in the joint fluid of a boy with chronic arthritis although no history of an attack of dysentery could be obtained and cultures from the joint fluid and stools were negative.

Although cases of dysentery septicemia are undoubtedly overlooked, routine blood cultures have proved very disappointing. Dudgeon[21] and his coworkers made blood cultures on 145 cases of acute dysentery in Macedonia during the war but failed to recover the organism. Fränkel made 49 blood cultures and in only one case obtained a pure culture of the "Y" dysentery bacillus. Kessel,[22] at the Los Angeles County Hospital, made 60 blood cultures with completely negative results. TenBroeck made bacteriologic studies of various organs at autopsy in 14 cases of dysentery with negative results. These figures corroborate the prevailing opinion concerning the rarity of dysentery septicemia and emphasize that the presence of the organism in the peripheral blood is of no practical aid in diagnosis.

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3875 Wilshire Boulevard

# SCLERODERMA

## Report of a Case With Sclerodactylia and Hemiatrophy

Robert H. McCrackin, M.D.
Edea, Cameroun,
West Africa

ALTHOUGH cases of scleroderma, or hidebound skin, presenting the clinical picture of the adult type have been reported at all ages in life, from Cockayne's case[1] in a seven-month-old infant with scleroderma and sclerodactylia of the adult type with some fibrous myositis (of antenatal origin) to the commoner time for its occurrence during the later decades in life, it is a rare condition, particularly in children.

Some conception of the low incidence of scleroderma in children can be obtained from the fact that Dr. Howard Fox[2] went through the records of about 5,800 cases of miscellaneous diseases at the Nursery and Child's Hospital and found only one case of scleroderma. This case occurred in an infant, and since biopsy was not performed, he felt the condition could not possibly be differentiated from sclerema. He found that the records of about 75,000 skin diseases at the University of Bellevue Clinic contained only one case of scleroderma in a child, a boy, aged fourteen years, in whom the condition had been present since infancy.

### DEFINITION AND ETIOLOGY

Scleroderma is described by Ormsby[3] as being a disorder characterized by induration of the skin in localized patches or diffuse areas frequently associated with atrophy and pigmentation. When the fingers are involved it is known as sclerodactylia. Two types occur fairly distinct as to distribution, the diffuse and the circumscribed, both types occasionally being seen in the same patient. As to age groups, two types are well differentiated, the so-called primary scleroderma occurring before birth and during the first two years of life, which is the more common up to the beginning of the period of the second dentition. In the later years of childhood the cases usually are of the adult type, the majority of all cases falling in the third and fourth decades of life. It occurs more commonly in the female sex, the proportion being 3 to 1. In sclerema neonatorum, with which scleroderma should not be confused, the sexes are equally liable. In Cockayne's tabulation of 102 cases in children under fourteen years of age, collected from the literature, there were 28 boys (29.2 per cent), 68 girls (70.8 per cent), and 6 in whom the sex was not specified.

Throughout most of the case studies which have been made, there is found to be a predominance of scleroderma in the Jewish race.

The exact etiology of scleroderma is still somewhat obscure although many contributing factors have been pointed to as precipitating the condition. Morphologic and functional changes of the endocrine glands, the thyroid in particular, have been said to play a part. This is based upon the disorders of the thyroid occurring in association with scleroderma such as hypertrophy, atrophy, sclerosis, and diminution of iodine content. The gland seems to be decreased in size more frequently than enlarged. The basal metabolic rate is variable in cases of scleroderma. It may be slightly lower than normal or higher or perfectly normal, but is usually within the normal limits. Roques,[4] in an analysis of thirty-one cases in which the state of the thyroid was mentioned, reported clinical modifications in the gland in twenty-two instances. The resemblance between myxedema and scleroderma has been frequently mentioned. The apparent success in the treatment of certain cases with the use of thyroid preparations probably accounts for a great deal of the blame's being placed upon a malfunctioning thyroid as the etiologic offender. At the present time, however, less confidence seems to be generally felt in this line of treatment unless there are definite symptoms of thyroid trouble.

Adrenal insufficiency has definitely been known to be present with scleroderma if not the causative factor in such cases as the one reported by Sequeira.[5] He describes a case of scleroderma in a twenty-four-year-old Polish Jewess with a hypotension of adrenal insufficiency. Scleroderma may also occur in association with Addison's disease.

The frequency with which calcium deposits are found in the soft tissues, particularly in the finger tips in sclerodactylia, and the fact that scleroderma may occur with a generalized calcinosis,[6] which cases may show improvement or cures following either a ketogenic diet or after parathyroidectomy, would indicate that hyperparathyroidism or some other parathyroid dysfunction may in some cases be the contributing factor, or an associated condition.

Scleroderma may follow various infectious diseases such as measles, tonsillitis, scarlet fever, diphtheria, pneumonia, and influenza. Trauma and exposure to cold appear to bring on certain cases. Emotional upsets, such as shock and grief, have been named as etiologic factors, as well as prolonged exposure to the sun's rays.

Scleroderma is found with relative frequency as an associated symptom of Raynaud's disease and, occasionally, of thrombo-angiitis obliterans.

Several observers have found a positive Wassermann reaction in a certain percentage of the cases inferring that syphilis may be a cause. Other observers find no larger percentage of sclerodermic patients with a positive Wassermann reaction than would be expected among the general population. However, the majority of syphilitic individ-

uals with scleroderma show improvement or a clearing of the skin condition under antisyphilitic treatment.

Ayers[7] has found arsenic in the urine in a number of patients suffering from scleroderma suggesting that this process may be a manifestation of arsenic poisoning in these cases.

The general conception of the majority interested in this subject seems to be that scleroderma is an angiotrophoneurosis due to disturbance either in the peripheral or central nervous system. This view is borne out by the presence early in the course of the disease of the symptoms of erythema, occasionally of paresthesias or transient attacks of local cutaneous asphyxia, and later of pigmentation. The attacks of Raynaud's disease, which often precede sclerodactylia, are also in accord with this view. The areas of skin involvement often correspond to segmental areas either of the cutaneous nerves or over spinal areas. The atrophic involvement usually found in the adult type, as hemiatrophy of the face or of the whole body and the association with organic nervous diseases, such as tabes dorsalis, as does occur, would further indicate a nervous origin of scleroderma.

Cockayne suggests a very logical theory that, in patients suffering from disease of the ductless glands in the presence of scleroderma, the disease of the skin and the ductless glands are probably both due to a disorder of innervation, in which case all of the above mentioned endoctrine disturbances would have to be regarded as concurrent findings rather than causative factors. He is also of the opinion that the cases of diffuse scleroderma with sclerodactylia and often accompanied by myositis are more probably due to a local infection of the skin or of the skin and muscles. Nearly all of the cases of primary scleroderma from prenatal life on through early childhood are in this group, etiologically. In the later years of childhood the majority belong to the group which are most likely due to some derangement of the sympathetic system.

Poussepp and Rives[8] report a case of sclerodactylia with scleroderma which seems to bear out this theory of the condition's being due to a sympathetic upset. A girl with glandular tuberculosis and manifestations of sympathetic hypertonus, as exophthalmos, inversion of the oculocardiac reflex, and dilatation of the pupils, developed atrophy of the phalanges with joint lesions at the age of eight years. The skin became involved, showing areas of depigmentation, dilatation of the veins, and local warmth. Histologic examination showed the characteristic lesions of scleroderma. It seems theoretically plausible that these changes may have been induced by the tuberculosis virus, to which the sympathetic system is peculiarly sensitive.

Oliver[2] and Michael[9] both agree with Hoffmann's belief that sufferers from diffuse scleroderma have unstable vegetative constitutions. He based this theory on the lack of general reaction to epinephrine in

thirteen cases of diffuse scleroderma and a lack of rise in the sugar curve after the administration of this drug. Controls in normal persons rarely acted in this manner. He believes that diffuse scleroderma may develop from shock, cold, trauma, syphilis, or other infections only in those who have an abnormal neuroendocrinologic mechanism.

### SYMPTOMATOLOGY

Since the condition is characterized by circumscribed or diffuse hardening, rigidity, and immobility of the skin, the symptoms vary with the areas involved, and then largely on a mechanical basis, except where atrophic changes of the muscles have taken place.

Usually there are no subjective sensations prior to the cutaneous manifestations though there may be neuralgic and arthritic pains or paresthetic sensations as the first signs in certain cases, especially those involving the extremities, according to Dr. Ormsby. In diffuse scleroderma the process develops insidiously, as a rule beginning about the extremities, face, neck, or trunk, with merely a feeling of stiffness as the earliest subjective sign. In most cases the earliest cutaneous changes are either infiltration or a peculiar edema. When edema occurs as the first sign, it may or may not show also an erythema. The case herein reported is of the type showing edema without erythema as the first sign. There may be areas of telangiectasis. When scleroderma is fully developed, the skin feels leathery and cannot be picked up because it is bound down to the underlying structures, hence the synonym "hidebound skin." At first there is no color change, but later the areas become depigmented taking on still later a *café-au-lait* or an old ivory hue. Still later in the evolution of the process the lesions may be bronzed or definitely brown, prior to resolution. The skin involvement may spread slowly or rapidly, covering local areas or the entire body.

When the face is the site of involvement, expression lines are effaced. If the eye regions are involved, there will be difficulty in opening and closing the eyes. Mastication may be interfered with. In extensive chest involvement respiratory movement may be curtailed. Joints of the body may be bound as to impair motion.

When the hands are involved, there is produced sclerodactylia or claw hand. Here, as elsewhere, the joints themselves are not involved, but there is contraction and fixation of the flexors of the hand and wrist. In many cases the skin of the flexor surface of the forearm becomes bound down to the underlying tendons and muscles, which themselves seem sclerotic with the loss of their normal pliability and elasticity.

It is difficult to determine accurately just what proportion of the cases of scleroderma is complicated by sclerodactylia. Up until 1919

there were reported fifteen cases of scleroderma in which there was made special mention of an accompanying sclerodactylia. This hand condition is often considered as characteristic of one form of scleroderma, the diffuse, symmetrical, atrophic type. Therefore, there are undoubtedly many cases of scleroderma reported in which sclerodactylia has been in the picture but not pointed out, being regarded as an expected part of the process rather than an entity.

Following the stage of edema or infiltration, there occurs varying degrees of atrophy of the underlying structures. The atrophy which develops in the majority of the cases of the adult type is usually less extensive than the areas of preceding edema or infiltration. Cases have been reported of hemiatrophy of the face, an atrophy of an extremity, and even a hemiatrophy of the entire body. The edematous stage lasts from a few weeks to several months, after which time the edematous fluid is absorbed, the skin shrinks, and the atrophies make their appearance.

Cockayne, in his analysis of 102 cases in children collected from the literature, found that the commonest form of the disease in childhood is that with isolated plaques or bands of induration. Diffuse scleroderma with or without sclerodactylia and sclerodactylia alone is much rarer. He states further that more than one example of complete hemiatrophy with scleroderma of the atrophic half of the body has been encountered. This is the condition with which I am convinced we are dealing in our case. While the same course of events in the process is found in children with scleroderma, the course is more often acute, and severe atrophic forms are less frequently seen, even though Cockayne in his series found many which were severe and atrophic.

In the primary scleroderma of infancy areas of scleroderma appear, which spread for a time, often coalesce with others, then undergo resolution, and disappear. According to Dr. Ormsby, the skin in the areas may be normal in color, bluish or brownish red. The trunk, particularly the lower part posteriorly, and the extremities are the areas most commonly involved.

Other varieties of scleroderma are described, such as the above mentioned circumscribed scleroderma, or morphea, with the single or multiple discrete, firm, smooth patches, lines or bands, which are either elevated or depressed and surrounded by a violaceous halo, the involution of which may be followed by atrophy.

Morphea guttata, or white-spot disease, is discussed in most dermatology texts under scleroderma. The unusual thing about this eruption is the absence of color, the plaques being chalky white or snow white and the distribution being chiefly on the anterior surface of the chest and on the neck and shoulders. Occasionally they may occur on the arms, forearms, and other parts of the body.

### PROGNOSIS

The outlook is variable. It is generally believed that the prognosis is very good in the primary scleroderma of infancy, the majority clearing up without residual findings. In children with the adult type the outlook is considered to be somewhat better than in adults, while some may terminate fatally by intercurrent infection. The process may stop at any time, and while the skin may soften and again return to its normal color, the sequelae depend upon the extent of the atrophic changes at the time of cessation of activity.

### PATHOLOGY

The histologic study of the skin in the case of Atwater[10] is representative of the usual findings reported in scleroderma. The report is as follows: "The skin showed considerable thickening of corium, the connective tissue of which showed dense and, in places, hyaline collagen. The epidermis was of normal thickness and contained in the basal layer more than the average amount of brown pigment. Immediately beneath the epidermis the connective tissue was of much more delicate structure. The collagen bundles were small, loose textured, and there were occasional apparently active fibroblasts. The coil glands were normal. There were a few normal appearing hair follicles in the specimen."

The pathologic changes are usually described as being those of exudation and swelling around the sweat glands, hypertrophy of connective tissue followed by atrophy of the vessels and epidermoid structures. When the fingers are involved there is absorption and atrophy of bone.

### X-RAY

Cases have been reported in which calcium concretions have been present in the fingertips in sclerodactylia and also in which generalized calcinosis with scleroderma[6] has been found. Atwater reviewed the cases of sclerodactylia reported with x-ray findings and reported his own case, finding that there is quite a typical appearance of atrophy, absorption, and eventually disappearance of the terminal phalanges, most commonly of the hands and sometimes of the feet. His own case showed a definite bone atrophy and absence of the tips of the terminal phalanges of the second to fifth fingers, inclusive.

Edeiken[11] reports three cases of scleroderma with sclerodactylia giving the x-ray findings. In these, all showed some absorption of the terminal phalanges, and two showed small calcareous concretions in the finger tips. He states that, while bone atrophy and absorption of the tips of the phalanges is common in Buerger's disease, Raynaud's disease, leprosy, and ainhum, as well as in sclerodactylia, from his own observations and a study of the literature he found that sclero-

dactylia is the only condition which will give the roentgenologic picture of calcareous deposits in the finger tips combined with bone absorption of the tips of the phalanges. These concretions are found to be composed of calcium carbonate and calcium phosphate and are densely opaque to x-rays.

In his article on calcinosis and scleroderma Kennedy[6] reports a case in a girl, aged six years, who was treated by ketogenic diet with good results. She came under "Type 2 Diffuse" in the following classification which he offers for cases of scleroderma with calcareous concretions.

Circumscribed

Type 1. The calcareous concretions of scleroderma *(en plaque)*.

Type 2. The calcareous concretions of scleroderma *(en bandes)*.

Diffuse

Type 1. Affecting women almost entirely (26 of 27 patients in reports found by Basch)—occurring as a rule in the course of Raynaud's disease and thyroovarian upset. The features are onset with a sclerodactylia, calcareous concretions with characteristic subcutaneous situation in the tissues of the digits, relative rarity of involvement of the muscles and skeleton, and slow evolution with relatively favorable prognosis.

Type 2. This group is characterized by the predilection for females. It is an affliction of the young, chiefly between the ages of eight and fifteen, designated by Basch,[12] whose work has been studied by Kennedy as chronic edematous scleroderma with "sclerotendonitis" and "scleromyositis" exhibiting calcification which localizes characteristically in the proximal portion of the extremities and trunk superficially and deep.

In the cases showing calcareous deposits, the blood calcium is usually normal or only slightly elevated.

## TREATMENT

Many things have been tried in the treatment of scleroderma in the line of drugs, opotherapy, and, in recent times, surgery, with variable results. The most important single thing for the majority of patients would be the maintenance of nutrition and, if the patient is a child, growth, by a nutritious diet, cod liver oil, and perhaps iron tonic.

If there is found some condition associated with, or a definite underlying cause for, the scleroderma, this should certainly be treated, such as antiluetic treatment for those showing a positive Wassermann re-

action, the treatment of hypothyroidism if it is present, or glandular therapy in cases showing signs of specific endocrine dysfunctions.

Many gland preparations have been used in times past. Roques reports success with thyroid administration in 63.7 per cent of the cases and states that this treatment should be begun early and should consist of small doses continued over a long period of time. The results with thyroid therapy are, in general, not striking enough to counterbalance the difficulty of evaluating results because of the fair percentage that clears up without it; thus this line of therapy does not hold the place that it did at one time in the treatment of scleroderma. In Roques' report suprarenal extract had been used with benefit in some cases. Pituitary extract had failed to show results in four cases in which it was tried. Testicular and ovarian extracts have been used almost without success. Schwerdt, in five cases of localized scleroderma, reports promising results with a mesenteric gland preparation.

Parathyroidectomy has been performed with good results; also sympathetic ganglionectomy has been coming into favor recently in certain selected cases.

Locally it is well to use massage; alternating hot and cold douches are of value in attempting to promote circulation and encourage resolution. In massaging the affected parts daily, inunctions of cod liver oil, lanolin, lard, vaseline, or slightly scented neat's-foot oil may be used (Ormsby). A small amount of ammoniated mercury or salicylic acid may be added.

Thorium X emanations incorporated in an ointment base containing eucerin has been used by Epstein.[13]

### REPORT OF CASE

A. W., white female, aged five years and five months, was first seen by me in Chicago, on Jan. 4, 1936, with the major complaint of a flexion deformity of the fingers of the right hand and also numerous skin spots and areas of thickening with certain color changes, chiefly over the right half of the body.

The informant, the patient's father, gave the history that the first symptom to appear was the inability to open the hand which was discovered at play by an older brother on May 19, 1935. So far as the parents were able to determine, the condition of the hand when first noticed remained static until now, but the entire arm seemed to have become smaller during the past few months. In the process the third, fourth, and fifth fingers were the ones chiefly involved. The index finger could not be bent back as far as the corresponding finger of the left hand. The thumb was quite normal.

After some weeks there followed the appearance of depigmented areas over the anterior chest, the flexor surface of the right arm and forearm, the lower abdomen, beneath the right ramus of the jaw, and a small area over the right eye. There had been no redness or violaceous colored halos around the lesions at any time as described in morphea.

Then there appeared two plaques in the skin well described in the father's own words: "The white areas appeared in late July and August. We thought at first it was the way she had tanned in the sun. Then in September while massaging and soaking her arm in hot and cold water, we noticed a yellow skin spot on the inside of her right arm at just about the spot of the muscle (the medial aspect of the belly of the biceps). It seemed thick and leathery. Then we next noticed this same sort of a spot on her chest. It showed sort of shiny first in the sunlight; then it seemed to raise up as it is now. This spot spread over an area of 2 by 3 inches (5.08 by 7.62 cm.), not solid but spotted. The spots did not seem to appear where the white places were, except on the chest, which was more or less bleached out all over. This seemed to appear more on the right side, much more so, than on the left."

In December an uncle of the child first noticed that the right side of the patient's face was smaller than the left, particularly that the lower half seemed "more drawn up." This was preceded by the discoloration underneath the right margin of the jaw. At this time there were no lesions on the face except for the small spot on the forehead.

Just recently there has been a feeling, objectively, of thickness of the skin covering the anterior right thigh, without any color change.

There have been no subjective symptoms whatsoever in connection with these skin and muscular changes.

The past history did not vary from the story of a perfectly normal child. There was nothing relevant in the family history. The parents are both living and well. There have been three pregnancies, all of which were full term. The two brothers, aged sixteen and eleven years, were in good health. The patient has a normal birth history, weighing 7 pounds and 6 ounces (3.345 kg.). She weighed 15 pounds (6.804 kg.) at six months, 20 (9.072 kg.) at a year, and during the past year the weight has fluctuated between 33 and 35 pounds (14.968 and 15.876 kg.). She was breast fed for two months, and then was placed on a cow's milk-karo syrup formula. Orange juice and cod liver oil were started at one month and given regularly. There were two teeth at six months and ten days with an eruption of all the temporary teeth by the end of the second year. She was running "everywhere" at twelve and a half months and had quite a vocabulary at eighteen months.

Of the contagious diseases of childhood, the patient has had only measles (March, 1935.) She has not been vaccinated, nor has she had any other immunization. The surgical history was negative.

As to habits, the appetite was only fair; bowels were regular; patient slept well, seemed stable emotionally and had always been very active, preferring a romp outdoors to indoor confinement.

*Physical Examination.*—The physical examination revealed a thin but fairly well-developed white girl, who was cooperative and apparently happy, measuring 42½ inches (107.94 cm.) in height and weighing 35 pounds (15.876 kg.). Except for the sclerodermic and atrophic changes under discussion, the regional examination revealed nothing abnormal. The eyes reacted to light and accommodation. The ears and nose were normal. The teeth were in good condition with three fillings and with normal appearing gums and buccal mucosa. The tonsils were of medium size with no superficial evidence of being infected. The child breathed through the nose and spoke with the voice of one free from any nasal obstruction. There was no cervical lymph gland enlargement. The thyroid seemed to be of normal size. The heart was normal, and the lung fields were clear. There was no abdominal tenderness, and no abnormal masses were felt. The genitals were normal.

The distribution of the skin lesions was as follows: There was a small white spot over the right eye about a centimeter in diameter midway between the eyebrow and

the hairline of the scalp. There was a band of sclerodermic involvement of the neck beneath the right ramus of the mandible and roughly parallel to it extending from the inferior tip of the lobe of the right ear with the circumference of the neck to the midline anteriorly at a point 1 inch (2.54 cm.) beneath the mental process and varying in width from ⅛ to ⅝ inches (3.17 to 15.85 mm.), elevated, indurated, and of an ivory color.

The most extensive and deepest involvement was that of the entire flexor surface of the right upper extremity. The skin of the palm and forearm (flexor surface) could not be picked up between the fingers. It had a firm feeling to the touch and seemed to be completely bound down to the underlying structures. The involvement of the arm was more in the form of a plaque which lay with the long axis of the

Fig. 1.—Case of scleroderma showing the hemiatrophy of the right side of face.

arm over the medial portion of the biceps muscle anteriorly to the inner margin, overlying the brachial artery. This plaque was elevated and measured ¾ by 2½ inches (1.9 by 6.35 cm.). This region was considerably warmer to the touch than the surrounding area. The color of these lesions on the arm and forearm could best be described as being a dirty yellow. Over the yellow areas, even more than the depigmented spots, the skin was intensely smooth and atrophic, there being no hairs or hair follicles that could be seen. There seemed to be no sensory changes in the affected areas.

The anterior chest region, in an area bounded roughly by the clavicles, the anterior axillary folds, and an imaginary transverse nipple line, inferiorly, was covered with areas of depigmentation varying in size from a pinhead to a half inch (12.70 mm.) with a tendency to become confluent and to form irregular larger areas. In the mid-

sternal region with the long axis of the body there was an ivory-colored plaque similar to the one above described in every respect, oval in outline, and measuring ⅝ by 1¼ inches (0.95 by 3.17 cm.). Across the lower abdomen there were scattered discrete areas of depigmentation, more dense in the immediate suprapubic region.

Over the back and gluteal regions there were widely scattered small areas of depigmentation, most of them about 3 to 5 mm. in diameter.

The skin over the entire anterior surface of the right thigh extending from the right inguinal region to the patella had a very peculiar feeling when picked up in the hand. It seemed vaguely edematous or thickened without pitting on pressure. The color of the skin in this area was perfectly normal.

Attention to the atrophic changes revealed that the right side of the face from the midportion of the cheek downward was smaller than the left (Fig. 1). The right ala of the nose was smaller and described a slightly higher arch on that side. When the mouth was held in repose, there was visible a muscular inequality between the two halves of the mouth, with some deficiency about the right angle.

Fig. 2.—Sclerodactylia of the right hand showing the maximum extension possible.

The third, fourth, and fifth fingers of the right hand were flexed (Fig. 2) in about the position in which the hand is ordinarily carried in walking and could not be extended manually except by flexing the wrist, and then only partially. Upon attempts to extend the fingers the flexor tendons became prominent, showing that there was a definite shortening of this group of muscles and that, as usual in this condition, there was no joint involvement back of the difficulty. The active and passive movements of the index finger and thumb seemed normal, except that the former was somewhat more resistant to forceful extension than the corresponding finger of the left hand. There was a noticeable decrease in the size of the entire hand and forearm. The element of disuse could not enter here in view of the fact that the child had never favored the involved extremity in any way, writing and drawing with it quite as much as any right-handed child. When the arm was abducted, there was drawing of the anterior axillary fold due to skin shortening.

*Course.*—The patient was again seen three months later on April 8 and showed certain changes, some of progression and some of resolution of the process. Instead of the small white spot seen on first examination over the right eye there were two concentric arcs of scleroderma which seemed to be following cutaneous nerve

branches. They were each ⅝ inch (15.85 mm.) wide and were situated 1 inch (2.54 cm.) apart. The longer of the two, situated laterally, began directly over the eye a half inch (12.70 mm.) above the eyebrow and curved upward and slightly outward extending ¾ of an inch (19.05 mm.) above the hairline. The other band extended from 1 inch (2.54 cm.) above the inner end of the eyebrow and likewise curved upward and outward ending ½ inch (12.70 mm.) above the hairline. There was a complete absence of hair where the ends of these bands extended into the scalp region. These areas were of the color of old ivory and showed atrophy of the underlying structures as evidenced by a definite depression along their entire course.

The condition of the hand seemed unchanged except that the index finger could not be extended quite so far as previously. The skin of the palm and of the forearm seemed definitely more pliable, particularly the upper two-thirds of the forearm.

Fig. 3.—X-ray films of hands, sclerodactylia involvement of the right.

A new plaque had developed between the left nipple and the left sternal margin, oval in outline, and in a transverse direction measuring 1½ inches (3.81 cm.) with an average width of ½ inch (12.70 mm.). Another small plaque had developed in the region of the left biceps near the midpoint and medially.

The skin of the lower abdomen had returned to normal color except for a mottled area of depigmentation in the right lower quadrant about 1½ by 3 inches (3.81 by 7.62 cm.).

Since the last visit there developed an area of telangiectasis over the right scapula inferior to the scapular spine and extending medially to the midline.

The skin of the anterior thigh lost the feeling of thickness but has the flaky depigmentation spots which have been most noticeable over the trunk. The skin over the entire length of the tibia anteriorly was shiny and smooth. There was no marked change in pigmentation except from the edema. There was definite pitting of the skin when pressed against the tibia.

The circumferences taken of the extremities at corresponding levels show a definite soft tissue atrophy of the entire right upper extremity and of the right thigh. The measurements are as follows:

| | Right | Left |
|---|---|---|
| Midarm | 5⅝ in. (14.28 cm.) | 6⅛ in. (15.56 cm.) |
| Midforearm | 5 1/16 in. (12.86 cm.) | 5½ in. (13.97 cm.) |
| Wrist | 4⅛ in. (10.48 cm.) | 4 7/16 in. (11.27 cm.) |
| Palm | 4¾ in. (12.06 cm.) | 5 in. (12.70 cm.) |
| Thigh (at gluteal fold) | 11 in. (27.94 cm.) | 11½ in. (29.21 cm.) |
| Midthigh | 10⅝ in. (26.98 cm.) | 11 in. (27.94 cm.) |
| Suprapatellar region | 8½ in. (21.59 cm.) | 9 in. (22.86 cm.) |
| Calf | 8 7/16 in. (21.43 cm.) | 8¼ in. (20.95 cm.) |
| Ankle | 5¾ in. (14.60 cm.) | 5¾ in. (14.60 cm.) |

It is interesting to note that the skin of the right thigh, having passed from the edematous stage to the atrophic, falls into the expected measurement relationship with the corresponding part, while the leg of the same extremity is in an earlier stage and, as a result, measures slightly more in circumference owing to the edema, than the normal left leg.

*Laboratory Findings.*—The laboratory study was made upon the second visit of the patient in April, 1936. Blood examination showed 80 per cent hemoglobin (Newcomer), 13.5 grams, with an erythrocyte count of 5,180,000. There was a total leucocyte count of 10,550 with a differential of polymorphonuclear leucocytes, 50 per cent, lymphocytes, 40 per cent, monocytes, 5 per cent and eosinophiles, 5 per cent. The urine was acid in reaction and negative throughout to both chemical and microscopic study. The blood calcium was 10.3 mg., and the phosphorus 4.3 mg. per cent.

*X-Ray Findings.*—The x-ray study was made by Dr. W. E. Anspach who reports:

"Films of both hands and other long bones, which include the greater portion of the trunk, fail to show x-ray evidence of calcium deposits in the soft tissues. The bones on the whole have normal texture and density, and there is only slight general loss of density of the bones of the affected right hand (Fig. 3) as compared with the normal left hand.

"The lung fields and heart appear to be within the limits of normal."

## DISCUSSION AND SUMMARY

There has been presented in this paper a general discussion of the rare condition known as scleroderma, the adult type of which seems to be best explained upon the basis of an abnormal sympathetic endocrinologic mechanism and which is precipitated by such conditions as shock, cold, trauma, syphilis, acute infections, etc. There is the primary scleroderma, which occurs from prenatal life on through early childhood, but this is more probably due to a local infection of the skin. The case reported here is of the adult type of scleroderma in a child aged five years and five months, who presents, in addition to the skin lesions of scleroderma, a hemiatrophy of the body, or at least an atrophy of the right side of the face (including forehead, cheek, nose, and mouth), the right upper and the right lower extremities, and sclerodactylia of the right hand.

Out of as nearly a normal history as one often finds, measles is the only illness which might have precipitated the scleroderma; it is on the long list of causative factors to which the development of scleroderma has been attributed. This attack of measles preceded the onset of the sclerodermic process by eight weeks.

This case seems to be following the rule of this condition in that each case is a law unto itself, clearing up in areas while other regions continue on to atrophy of the underlying tissues. Just what the ultimate outcome will be it is very difficult to say.

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L'HÔPITAL DE SAKBAYEMÊ

# TECHNICS FOR MEASURING INFANTS

HELEN L. DAWSON
IOWA CITY, IOWA

THERE seem to be nowhere in the literature adequate directions for measuring infants. This is a problem in which the mere definition of the particular measurement and the description of the instruments to be used are not sufficient, as anyone well knows who has attempted to apply to infants the measuring technics that are found in books of anthropometry. Such standard descriptions, while they are adequate for work on adults, leave much to be desired when they are applied to infants. In the few articles available, which give directions for measuring infants, the authors fail to mention the difficulties or to caution against some of the common posture factors which are found in this age period and which tend to introduce unnecessary errors into the data.

In this paper the author will describe the technics which are being used at present in measuring infants at the Iowa Child Welfare Research Station. An attempt will be made to anticipate some of the difficulties which may be encountered and to discuss some of the problems involved in measuring at this early age level. It is hoped that this paper, in which a statement of one method is given, will help to stimulate interest in the standardization of the technics at present being used in working with infants.

## INSTRUMENTS

The various instruments that are used and the measurements that are taken with each one are listed below:

- Measuring board for infants
  - Crown-heel length
  - Crown-rump length
- Paper measuring scale
  - Standing height
  - Sitting height
- Large sliding calipers
  - Head length
  - Head breadth
  - Shoulder breadth (bideltoid)
  - Chest breadth
  - Chest depth
  - Hip breadth (bi-iliac and bitrochanteric)
  - Elbow breadth
  - Knee breadth
- Metal tape
  - Head circumference
  - Chest circumference
  - Arm
  - Forearm
  - Thigh
  - Calf
- Fat calipers
  - Chest front
  - Chest back
  - Arm front
  - Arm back
  - Suprascapular
  - Suprailiac
- Scales
  - Weight

From the Iowa Child Welfare Research Station, State University of Iowa.

DESCRIPTIONS

*The Measuring Board for Infants* (Fig. 1*A*).—This board was designed by Dr. Bird T. Baldwin and was made in the manual training shop at the State University of Iowa.

> The scale is one meter in length, with an additional margin of 4.5 centimeters at the one end. The width is 20.5 centimeters, with standardized buttonwood millimeter scales on either side. The vertical plane for the head rest is 15 centimeters at its greatest height, and the sliding vertical plane is attached to a brass rod which moves freely in a brass groove in such a manner that the millimeter reading may be taken from either side. The board is made of inlaid walnut and buttonwood and the standards on which it rests when in contact with the table are covered with heavy felt. The scale is accurate and portable.*

In addition to the 15 cm. sliding vertical plane, it is necessary to have a second one, 8 cm. high, for very small children whose thighs are too short to allow the knees to flex properly when the 15 cm. plane is used. These two planes are interchangeable, and the one used will depend solely on the size of the subject.

*Paper Measuring Scale.*—This scale is the Baldwin modification of the Broca plane. In describing it Dr. Baldwin states:

> The plane consists of a strip of the best type of inextensible and unshrinkable paper, one meter long and twelve and a half centimeters broad, with the metric divisions on the right edge of the scale in centimeters and millimeters, and the English on the left edge in feet, inches and fifths of an inch, and with a margin on each side of the scale and also at the top and bottom.†

This scale is fixed to a stationary vertical board and is used for taking the height and sitting height measurements.

*The Square.*—The square, which has been constructed in the university carpentry shop, consists of two pieces of seasoned walnut, 18 cm. by 13 cm., joined at right angles. Within this angle and in the midplane a third piece of wood, in which an opening has been cut to serve as a handle, is joined to the two pieces mentioned above and serves to strengthen the square. It is used in taking both standing and sitting height. One surface of the square is held against the vertical measuring board and brought down until the other surface is in firm contact with the child's head. The reading is then taken from the measuring scale at the lower edge (angle) of the square (Fig. 1*B*).

*The Bench.*—The bench which is used in taking the sitting height has also been constructed in the university shop. The one suited to young children is 30 cm. high, 20 cm. wide, and 25 cm. long (Fig. 1*C*).

*Large Sliding Calipers.*—This instrument, also known as the Hrdlička compass, was made in Washington for the Iowa Child Welfare Research Station and was tested by the Bureau of Standards. It is light, durable, and accurate (Fig. 1*D*).

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*Baldwin, Bird T.: The Physical Growth of Children From Birth to Maturity. Univ. Iowa Stud., Stud. in Child Welfare 1: 18, 1921.

†Baldwin, Bird T.: The Physical Growth of Children From Birth to Maturity. Univ. Iowa Stud., Stud. in Child Welfare 1: 15, 1921.

*Metal Tape.*—A steel tape graduated in millimeters is used.

*Fat Calipers.*—Special calipers, manufactured by the Kny-Scheerer Company, New York City, are used for taking measurements of the subcutaneous tissue (Fig. 1*E*).

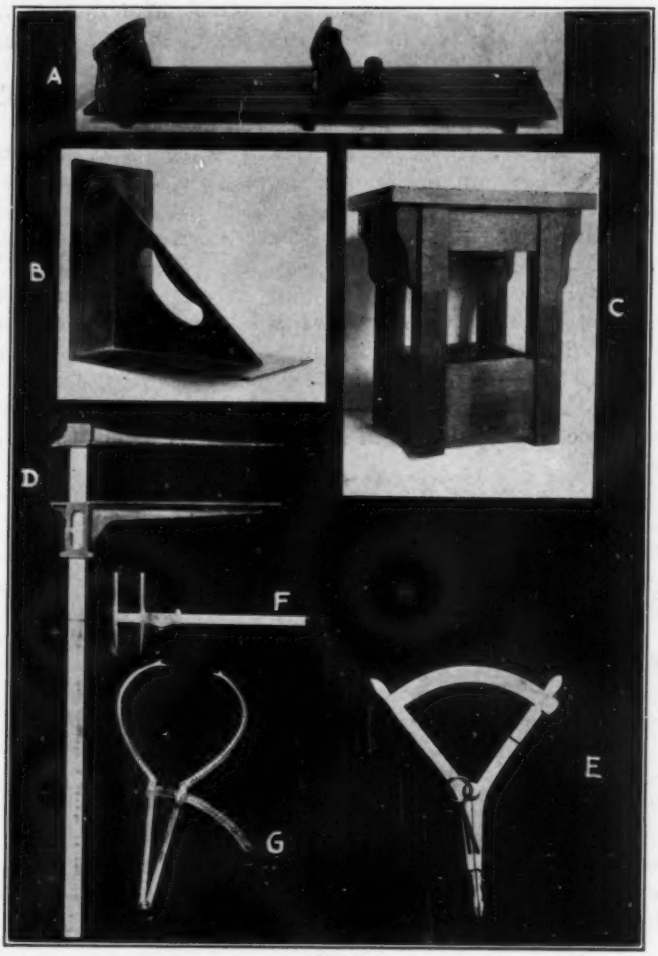


Fig. 1.

*Scales.*—Fairbanks scales which are graduated in both pounds and kilograms are used in taking the weight.

## MEASURING TECHNICS

The technics described below are applicable to children from birth to three years of age. All measurements are taken with the infant nude,

and in cases in which the measurement is taken on only one side of the body, the left side is always used. In working with children of this age the temperature of the room should be between 82 and 85° F.

*Lengths*

*Crown-Heel* (Fig. 2).—Age Range: From birth to two years, six months.

Instrument: Measuring board for infants.

Posture: Reclining; head in the Frankfort plane; head and body in a straight line; thighs and legs extended; feet flexed.

Technic: The subject lies on his back with the vertex of his head touching the stationary, vertical upright at the end of the measuring board. The legs are extended and the feet flexed. The movable, vertical upright is then brought up firmly two or three times in succession against the soles of the feet, and the reading is taken.

Comments: In measuring very young subjects, or older children who are not cooperative, an assistant will be found necessary to see that the head of the subject is in contact with the board and that the head and the body are in a straight line. The measurer places one hand on the child's knees in order to insure complete extension of the legs and with the free hand manipulates the sliding upright as indicated above.

In measuring very young children, who have not yet developed a lumbar curve, there will be difficulty in getting the legs extended. In complete extension of the legs a compensatory curve will be produced in the vertebral column. Since this procedure will be painful to the child, it should be done as rapidly as possible.

In older children, who are objecting to the position on the measuring board, the measurer must watch to see that the subject does not arch his back and shorten his total length in this manner. If he does, the condition may be corrected by flexing his thighs on his abdomen, then again extending the legs and measuring immediately.

*Crown-Rump* (Fig. 3).—Age Range: From birth to two years, six months.

Instrument: Measuring board for infants.

Posture: Reclining; head in the Frankfort plane; head and body in a straight line; thighs flexed so that the anterior surfaces of the thighs are at right angles to the horizontal base of the measuring board; legs flexed.

Technic: The subject lies on his back with the vertex of his head touching the stationary, vertical upright at the end of the measuring board. The thighs and legs are flexed and the movable, vertical upright is brought up two or three times in succession against the buttocks with a firm pressure, and the reading is taken.

Comments: Care should be taken that the thighs are flexed the right amount each time. In cases where the thighs are flexed more than

90 degrees, there will be a change in the curvature of the vertebral column; when the thighs are flexed less than 90 degrees the posterior parts of the thighs will interfere with the measuring. Both of these conditions will introduce an error into the measurement.

*Standing Height* (Fig. 4).—Age Range: From two through three years.

Fig. 2.

Fig. 3.

Instruments: Paper measuring scale (modification of the Broca plane) and square.

Posture: The subject stands erect, feet close together and flat on the floor. The back of the head, upper part of the back, buttocks, and heels should be in contact with the wall to which the measuring scale is attached. The arms hang at the sides in a natural position. The head is held in the Frankfort plane.

Technic: After placing the child in the correct position, the measurer holds the child's chin so as to maintain his head in the Frankfort plane. The square is held in the free hand and is brought firmly down against

the head two or three times. Sufficient pressure is used to feel the impact of the skull. The reading is taken from the last position.

Comments: Unless they are closely watched, there is a tendency for young children to rise on their toes just as the measurer brings the square down against the head. The assistant should check to see that the child is standing with the feet flat on the floor and that the knees are straight.

Error may be introduced if the square is tipped either to right or left (in the sagittal plane). This may be avoided by lining up one edge of the square with the edge of the measuring scale.

*Sitting Height* (Fig. 5).—Age Range: From two years through three years.

Instruments: Paper measuring scale (modification of the Broca plane), square, and square or oblong bench with a horizontal seat.

Posture: Sitting position, with back of head, upper part of the back, and sacral region of the back in contact with the board on which the measuring scale is attached. Children whose feet will touch the floor should cross the ankles, spread the knees apart, and relax the legs. The head is in the Frankfort plane and the arms hang at the sides.

Technic: The subject sits on a horizontal and resisting seat in the above position. The back edge of the seat should be in contact with the vertical board to which the measuring scale is attached. The head is held in the Frankfort plane by the measurer who grasps the child's chin and holds it firmly. The measurer holds the square in his free hand and brings it down against the head two or three times, using sufficient pressure to enable him to feel the impact of the skull. The reading is taken from the last position.

Comments: There is a tendency for children (particularly older ones) to contract the gluteal muscles and thus increase the measurement of sitting height. This is easily avoided if the knees are spread apart, the ankles crossed, and the legs relaxed.

Care must be taken to see that the child is sitting as far back on the bench as possible (the back edge of the bench must be in contact with the vertical board on which the measuring scale is attached). At times children tend to slide forward on the bench into a position which will produce a curve in the vertebral column and thus give a smaller measure of sitting height.

*Head Length.*—Age Range: From birth through three years.

Instrument: Large sliding calipers.

Posture: Sitting or standing.

Technic: Children who are too young to follow directions and older ones who refuse to do so must have their heads held firmly during the measuring. The person assisting the measurer grasps the child's head at the base of the skull with one hand and with the other hand takes a firm hold on the chin. The chin is held in the palm of the hand

with the thumb and the second and third fingers on opposite sides of the mandible. The fourth and fifth fingers are flexed under the chin to prevent the child from lowering his head. After the head has been stabilized in this manner, the measurer grasps the tip of the immovable blade of the calipers and places it just over the glabella. The tip of the movable blade is then brought into contact with the back of the child's head at the point which is farthest from the glabella and in the midline of the skull. The pressure used is very firm. The reading is taken several times to insure the accuracy of the measurement.

Fig. 4. Fig. 5.

Comments: Children between the ages of eight and eighteen months often object to having their heads held, and they may struggle to free themselves. If this occurs, the person holding the child must be very careful that the child does not jerk his head up and force the blade of the calipers into his face. Speed on the part of the measurer will help greatly.

### *Breadths*

*Head Breadth.*—Age Range: From birth through three years.

Instrument: Large sliding calipers.

Posture: Sitting or standing.

Technic: When children are too young to follow directions or when older ones refuse to, the person holding the child places his hands

(palms open) on either side of the child's head at a level with the ears and holds it firmly. Since this is a measure of the greatest transverse diameter of the skull, the measurer places the tips of the calipers just above the ears of the child, keeping the blades parallel, and using a firm pressure. He moves them forward and backward, repeating the above technic until he is positive that the maximum breadth has been measured.

Comment: In little girls where the hair ribbon or other similar device for fastening the hair interferes with the blades of the calipers, it should be removed and the blades allowed to come into contact with the head.

Fig. 6.

*Shoulder Breadth* (*Bideltoid*) (Fig. 6).—Age Range: From birth through three years.

Instrument: Large sliding calipers.

Posture: Sitting erect; with arms down and elbows held tightly against the sides of the body.

Technic: The tip of the immovable blade of the calipers is applied to the arm, over the deltoid muscle opposite the head of the humerus. The rod of the calipers should be in a horizontal plane at the same level as the heads of the humeri. The tip of the movable blade is brought against the opposite shoulder over the deltoid muscle. Firm pressure is used, and the reading is taken several times; the mean is recorded.

Comments: Shoulder measurements are the least reliable of any of the measures of growth. The shoulder girdle is loosely articulated and extremely mobile, and this, in addition to variability in posture, re-

sistance of the individual who is being measured, and the amount of pressure used in measuring, tends to influence the measurement and to introduce errors. After experimentation with infants, the above combination of posture and technic was found to give the most reliable results.

Fig. 7.

Fig. 8.

Care should be taken to see that children who object to being measured do not hunch their shoulders, for this will narrow the shoulder width.

If the blades of the calipers are warmed slightly, the infants will object less than if they are very cold.

*Chest Breadth and Depth* (Figs. 7 and 8).—Age Range: From birth through three years.

Instruments: Large sliding calipers.

Posture: Sitting; the trunk held erect with arms relaxed and hanging at the sides.

Technic: Breadth—The blades of the large calipers are applied to the sides of the chest at the level of the xiphoid process. The pressure should be firm and the reading taken several times as a check on the amount of pressure which is used.

Depth—The measurement of chest depth is taken at the level of the xiphoid process. One blade of the calipers is placed over the xiphoid process, and the other blade is applied to the back of the thorax, the instrument being held so that the plane of the blades is at right angles to the vertical axis of the thorax.

Comments: Since crying influences this measure, every effort is made to have the child quiet at the time the measurement is taken. Toys, particularly those that make noise, are found useful in attracting the child's attention. If it is impossible to quiet the child, the measurement should be taken, nevertheless, and a note made on the card that the child was crying.

Chest width and, to a greater extent, chest depth are influenced greatly by the position of the child. If the child is very young and is allowed to slump when sitting, the abdominal organs push up and the ribs spread apart. This is particularly true in infants in whom the ribs are still very pliable. In newborn infants the upright position with a straight back is maintained through the help of the person holding the child.

The blades of the calipers should be warmed slightly before they are used.

*Hip Breadths* (*Bi-iliac and Bitrochanteric*) (Figs. 9 and 10).—Age Range: From birth through three years.

Instrument: Large sliding calipers.

Posture: Reclining position until children are able to support their own weight with the help of the person holding them; from that time on they are measured standing. In both positions the body is straight, the legs are extended, and the feet are held close together.

Technic: Bi-iliac—The person measuring first locates the crests of the ilia by palpation; then the blades of the calipers are placed over the crests and are brought together with very firm pressure. This is done several times before the reading is taken in order to check the accuracy of the measure.

Bitrochanteric—The same technic is used in taking this measurement after the trochanters have first been located by palpation.

Comments: Care should be used in locating the points, and the blades of the instrument must be held parallel to one another and at right angles to the long axis of the body.

Children who are measured in the reclining position must have their thighs and legs fully extended.

Fig. 9.

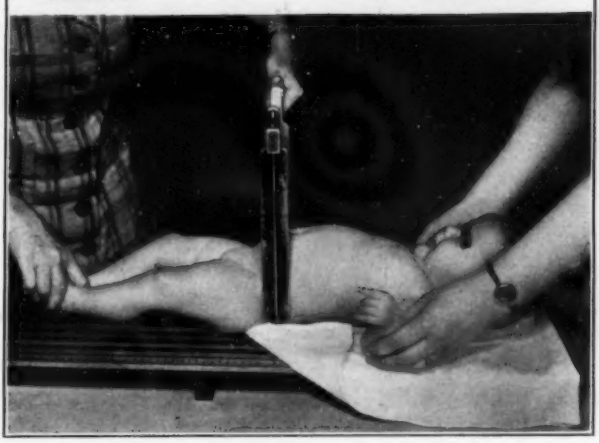

Fig. 10.

*Joint Breadths (Elbow and Knee).*—Age Range: From birth through three years.

Instrument: Large sliding calipers.

Posture: Elbow—The hand is in the supine position and the forearm is flexed until it forms about a 90 degree angle with the arm.

Knee—The sole of the foot should be parallel with the floor and the leg flexed on the thigh, forming about a 90 degree angle.

Technic: Elbow—The person holding the child grasps the left wrist, rotates the arm until the hand is in a supine position, then flexes the forearm. The measurer places the tips of the blades of the calipers on either side of the elbow so that the blades press upon the two epicondyles of the humerus. The pressure is very firm.

Knee—After the left leg has been flexed, the technic for measuring the knee is the same as that for the elbow. The tips of the blades of the calipers are placed over the two epicondyles of the femur.

Fig. 11.

Comments: In measuring both the elbow and the knee it is important that these joints be flexed at the time the measurement is taken. If they are not, the muscles will cover the epicondyles and give an erroneously large measurement.

### *Circumferences*

*Head Circumference* (Fig. 11).—Age Range: From birth through three years.

Instrument: Metal tape.

Posture: Sitting position with the head held erect.

Technic: First the tape is made into a circle with the two ends crossed and held by the measurer in such a manner that the circle can be made smaller by pulling on the free end of the tape. Enough of the tape is then released to make a circle which is larger than the child's head. The looped tape is slipped over the child's head, and the assistant

adjusts the tape posteriorly over that part of the occiput which is farthest from the glabella. While the assistant holds the tape in place posteriorly, the measurer adjusts it anteriorly above the supraorbital ridges, draws it tight, and reads the measurement.

Comments: When the infant objects to this measurement and struggles to free himself, the person holding him must be careful that the tape does not slip from the desired place, as he is responsible for keeping the tape in the right position posteriorly. It may be necessary for the person holding the child to place one hand under his chin in order to stabilize the head.

*Chest Circumference.*—Age Range: From birth through three years.

Instrument: Metal tape.

Posture: Sitting; lumbar region of the back straight or slightly concave anteriorly; arms relaxed and hanging at the sides; head held erect.

Technic: The measurer slips the tape around the child's chest and the measure is taken at the level of the xiphoid process. The pressure is such that the tape firmly contacts the skin, but only enough pressure is used to indent the skin very slightly. The extremes of inspiration and expiration are noted and the average recorded.

Comments: If the child is crying at the time the measurement is taken, the measurer holds the tape so that it can follow the movements of the chest wall during expansion and contraction which result from crying. Increase and decrease in size are carefully noted for a short period and the average of the extreme measures is then recorded.

Changes in the position of the head will result in a change in chest size; therefore the position of the head should be carefully checked.

*Girths of Extremities* (Fig. 12).—Age Range: From birth through three years.

Instrument: Metal tape.

Posture: Extremity extended.

Technic: All measurements are taken on the left side. The person holding the child keeps the extremity which is being measured extended. The measurer places the tape around the arm, forearm, thigh, or calf at the level indicated below. The pressure used is such that the tape merely contacts the skin firmly.

Level of Measurement for Arm—The tape is placed around the arm at a level that would bisect the midpoint of the biceps muscle transversely.

Level of Measurement for Forearm—The level is just below the elbow (the greatest circumference of the forearm).

Level of Measurement for Thigh—The tape encircles the thigh at the level of the gluteal fold.

Level of Measurement for Calf—The circumference is taken over the fleshiest part of the calf.

Comments: If the child's skin is moist, care must be taken to see that the tape does not stick to the skin and give an erroneous measure.

Fig. 12.

Fig. 13.

*Measurements of Skin and Subcutaneous Tissue* (Fig. 13).—Locations for measuring the skin and subcutaneous tissue are:

Arm (front)—This measurement is taken on the front of the left arm over the belly of the biceps muscle.

Arm (back)—The measurement is taken on the back of the left arm, opposite the location for measuring arm front.

Chest (front)—This measurement is taken on the left side about midway between the axillary line and the midline of the body and on a level with the seventh rib.

Chest (back)—This measurement is taken on the left side of the back, opposite the location for measuring chest front.

Suprascapular—The measurement is taken over the middle third of the spine of the scapula.

Suprailiac—This measurement is taken on the left side just above the crest of the ilium in the midaxillary line.

Age Range: Birth through three years.

Instrument: Fat calipers.

Posture: Sitting.

Technic: The measurer grasps the calipers in the right hand so that the movable arm is on the thumb side. The ball of the thumb is on the movable arm above the calibrated arc; the first and second fingers rest on top of the arc; and the other fingers remain on the outside of the stationary arm. With the thumb and forefinger of the left hand the measurer pinches up a double layer of the skin and subcutaneous tissue at the place of measurement, taking care not to include any of the underlying muscle. The long axis of the pinched-up tissue should run parallel to the long axis of the extremity of the body. The pinch should be taken by pressing inward with the ends of the fingers and at the same time pressing downward. The jaws of the calipers are opened wide enough to include this double layer of tissue and are pressed down over it to one side of the fingers; then the jaws are released, and the reading is taken from the calibrated arc. The fingers should retain their hold on the pinched-up skin and subcutaneous tissue with only enough pressure to prevent the tissue from slipping from between the blades. The measurement is taken several times before final recording to insure accuracy.

Comments: The pinched-up tissue over which the blades of the calipers are placed should represent a complete double layer of skin and subcutaneous tissue; none of the underlying muscle layer should be included.

### WEIGHT

The weight is taken without clothing.

### DISCUSSION

In conclusion, it may be well to mention briefly a few things of general interest in carrying out an infant-measuring program.

Because of the great variation in age of children being measured, it has been found that the measuring program could be carried on most efficiently with a minimum of three persons for the staff. This number includes one person who does the measuring, a second to hold the child, and a third person to record the data. It is advisable that the first two

people be trained to do the measuring, in which case they may take turns holding and measuring the infants. Where this is done and where the study is such that the same child returns periodically for measurements, it is suggested that the same person measure the child each time he comes.

The parent of the child is not allowed in the room during the measuring (with very few exceptions), but sits outside the room and observes the procedure through an observation window made in the door. This regulation was adopted after having first tried permitting the mother in the room during the measuring.

The room should be of moderate size, well lighted, and equipped with ventilating and heating facilities that are easily controlled. A small closet is necessary in which to keep the instruments. The furniture will include two tables, one on which the measuring board is placed and the other for the small instruments and for the convenience of the recorder. In addition the room will contain the scales, the vertical board with the paper measuring scale attached, and the measuring bench, several large chairs, and at least one small chair for the children. A clothes hamper is necessary since the children are laid on diapers when they are placed in the scales and on the measuring board, and these are changed for each child. The instruments and the board are wiped with an alcohol sponge after each child is measured.

Toys are an important and useful part of the equipment for the measuring room. They should be selected with the idea of getting things which will appeal to children over the entire age range. Rattles and rubber dolls or animals that make a noise are useful in diverting the attention of young children. In the older ages some simple toys of bright color which can be used in building are most entertaining. All toys should be large enough so the children cannot get them in their mouths, and the paint should be of some harmless material.

# TUBEROUS SCLEROSIS: ENCEPHALOGRAPHIC INTERPRETATION

RUSSELL N. DEJONG, M.D.
ANN ARBOR, MICH.

TUBEROUS sclerosis is a disease characterized by congenital abnormalities in certain tissues of ectodermal origin, especially the nervous system, skin, and retina. Due to the coexistent involvement of the nervous system and the skin, the condition is frequently spoken of as a neurocutaneous syndrome or as a congenital ectodermosis with associated nervous system involvement.[1] Certain of the visceral organs are occasionally involved as well. The disease is usually seen in children, and it is characterized clinically by a triad of symptoms consisting of retarded mental development, convulsive attacks, and so-called sebaceous adenomas. The term epiloia has also been suggested for this syndrome.[2, 3]

The cutaneous changes are of importance in the clinical recognition of the disease. They are characterized by multiple papular or nodular lesions which are most frequently distributed symmetrically, in a butterfly arrangement, over the bridge of the nose, the nasolabial folds, and the malar eminences. The individual lesion is spoken of as a sebaceous adenoma or a "nevus multiplex" of Pringle,[4] and it varies from yellowish pink to reddish brown in color, and from the size of a millet seed to that of a pea. Because of the fact that in most cases these lesions are not an adenomatous or hyperplastic condition of the sebaceous glands, but rather are lesions which belong to the nevoid group of disorders and consist of hyperplastic connective and vascular tissues, the use of the term nevus might be more justifiable.[5] The lesions, both from their appearance and their distribution, closely resemble those seen in acne rosacea. In addition to the involvement of the face, one occasionally sees skin manifestations over the back, shoulders, and the lumbosacral region. These resemble the lesions found in multiple neurofibromatosis,[6] and they may be of the following types: changes in pigmentation, areas of fibrous, hyperplastic skin of the type known as shagreen, nevi, or sessile, or pedunculated polyps.

The pathologic changes in the central nervous system in tuberous sclerosis are quite characteristic, and the clinical symptomatology is no doubt dependent upon the location of the changes. The brain is often small and hard, and pearly white to yellowish gray nodules may be found in the cortex, throughout the brain tissue, and in the ependymal

From the Department of Neurology, University Hospital, University of Michigan.

lining of the ventricles. These nodules vary in size and are seen most frequently in the frontal lobes, being rare in the brain stem and cerebellum.[7] When present within the ventricles the lesions give the appearance of bunches of grapes or "candle gutterings"[6] hanging down from the upper surface of the ventricles. Histologically these tumorlike accumulations are composed of large atypical cells surrounded by a dense glial network.[8] Certain of the large cells resemble giant nerve cells; others are thought to be primitive glial elements.[9] It has been suggested that these structures represent embryonal cells of the spongioblastic and neurcytic varieties which have failed to differentiate.[10] In addition to the skin and nervous system abnormalities, one may find tumorlike structures in the retina or the eyeball. The retinal tumors are of glial or vascular origin and have been referred to by Van der Hoeve as phakomata.[11, 12] Certain of the viscera, especially the heart, kidneys, pancreas, and liver, may contain cystic tumors or myomas.

The earliest recognition of the pathologic changes found in tuberous sclerosis was possibly that of von Recklinghausen (1862), who found sclerotic areas in the brain and myomas in the heart of a newborn child.[13] Credit for the first description of the syndrome is usually given to Bourneville, who in 1880 demonstrated islets of hypertrophic sclerosis over the cerebral hemispheres of a three-year-old girl with epilepsy, arrested physical development, hemiplegia, idiocy, and "acne rosacea" of the face.[14] Since then numerous descriptions of the clinical symptomatology and the pathologic changes in tuberous sclerosis have been reported in the literature. However, there are only three reports of pneumographic studies in tuberous sclerosis, and in none of these cases is the diagnosis incontrovertible. Stewart and Bauer have reported a case diagnosed as tuberous sclerosis in which the ventriculogram showed only dilatation of the lateral ventricles;[15] the patient did not have skin changes or tumors of the viscera. Postmortem examination of the brain showed diffuse hardening of the right cerebral hemisphere, which was felt to be a large area of tuberous sclerosis. A case with many congenital abnormalities such as cleft palate and cleft lip, but without sebaceous adenomas or recognized visceral involvement, was reported by Berkwitz and Rigler.[16] The encephalogram demonstrated bizarre deformities of the lateral ventricles, indicating gross cerebral abnormalities. Drake has reported a case without sebaceous adenomas or retinal tumors in which encephalographic studies showed three small discrete masses of calcification in the left occipital area and a similar single spot of calcification in the right cerebrum.[17] There was bulging of the right thalamus into the right lateral ventricle, and the basilar cisterns and subarachnoid channels were increased in size. The following case is of interest because it demonstrates encephalographic changes, similar to those found in Drake's case, in a patient in whom the clinical diagnosis of tuberous sclerosis is quite definite.

## REPORT OF CASE

C. G., an eight-year-old boy, was brought to the University Hospital because he failed to show normal mental development. His birth and early developmental history were normal, but he had been slow to walk and talk, and during the two years that he had gone to school he had shown little progress. At the age of one year he had had a convulsion which had lasted an hour and a half. Since this time convulsions had occurred whenever the patient had a fever. A facial eruption had gradually appeared since the age of four. There was no family history of mental retardation, convulsions, or of similar skin disorders.

The patient was a well-developed and well-nourished boy, but he was obviously retarded mentally. On the face were many reddish brown papular lesions which

Fig. 1.—So-called sebaceous adenomas present on the face in a butterfly distribution.

were present in a butterfly distribution over the bridge of the nose and the nasolabial region (Fig. 1). The lesions were of a rather brilliant erythematous color and varied from the size of a pinhead to the size of a glass-headed pin. They were soft, and there was no superimposed scaling. Some of them appeared to be confluent. On the back in the lumbar and sacral regions were lesions of a somewhat different type (Fig. 2). There was one nonpedunculated polypoid area 1½ in. by ¾ in. in diameter; this was smooth and soft, but there were superimposed papules and nodules. There were more masses of papules and nodules which tended to become confluent. These varied in color, and some were erythematous, some pink, and a few were white. There were three small, irregular, depigmented areas on the back, one on the right buttock, and one over the right hip. Some small nodules were also seen in the intergluteal fold. The general physical examination showed no other

abnormalities. Examination of the fundi oculi showed blurring of the disk margins with striations running out into the surrounding retina. There was a raised white lesion with a slightly yellowish tinge lying on the temporal side of the left disk. This appeared to be made up of a large number of small globular bodies. There was no evidence of inflammatory change, and the vessels were normal.

The neurologic examination showed, in addition to the above mentioned findings, some overactivity of the tendon reflexes, especially on the left. There was a moderately positive Babinski sign on the left, and Oppenheim's signs were positive bilaterally. There was no definite ataxia or dysmetria, although the patient's muscular coordination was inadequate, and he carried out skilled acts poorly. There

Fig. 2.—Polypoid and papulonodular lesions in the lumbosacral region.

was marked impairment of speech. The patient was jovial and appeared to be alert. He was very restless, and his attention was limited. A mental test recorded an intelligence quotient of 48. He failed especially in tests for memory, comprehension, and manual dexterity. Laboratory examinations on the blood and urine, including the blood Kahn test and nonprotein nitrogen, glucose, calcium and phosphorus determinations, were reported as being within the limits of normal. A skin tuberculin test gave negative results. The spinal fluid showed normal cytology, a total protein of 38 mg. per 100 c.c., and a three-plus globulin reaction. The colloidal gold curve was 0111100000.

Stereoscopic roentgen ray studies of the skull showed multiple calcium deposits in the brain tissue (Fig. 3). These were present on both sides of the midline but were more prominent on the right, and they were situated in the region of the superior margin of the third ventricle and above the pituitary fossa. The largest of

these deposits, as projected, was not over ¼ inch in diameter. There were no signs of increased intracranial pressure. An encephalogram was made, and 105 c.c. of cerebrospinal fluid were withdrawn and replaced by air (Fig. 4). The right lateral ventricle was found to be definitely larger than the left. There appeared to be soft

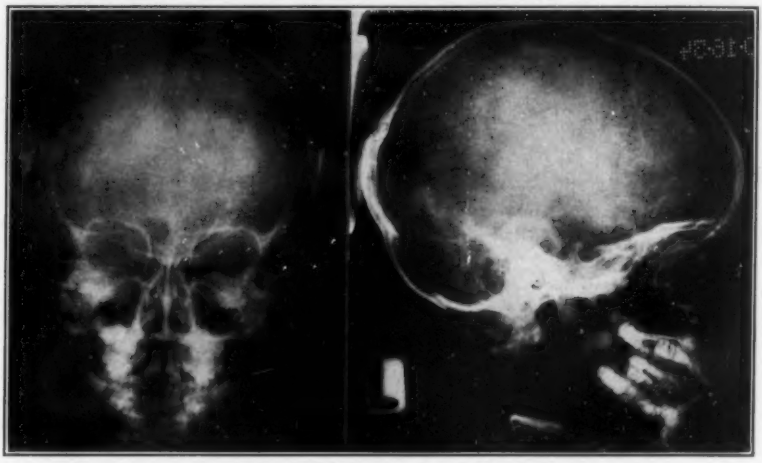

Fig. 3.—Anteroposterior and lateral roentgen ray studies of the skull showing calcium deposits within the brain tissue.

Fig. 4.—Encephalographic studies showing soft tissue masses and areas of calcification within the ventricles.

tissue proliferation along the floor of each lateral ventricle extending posteriorly from the region of the foramen of Monro. There were soft tissue tags extending into the posterior portion of the body of each lateral ventricle. These were felt to represent hyperplastic choroid plexus or other proliferated soft tissues. The larger calcium deposits noted in the skull films appeared to be in the region of the right

foramen of Monro. A rounded soft tissue shadow containing some calcium was seen to protrude down into the upper half of the third ventricle. The aqueduct and fourth ventricle did not appear to be abnormal, and approximately normal amounts of air were present in the basilar cisterns and the subarachnoid channels.

## CONCLUSIONS AND SUMMARY

Tuberous sclerosis is a congenital disorder of certain ectodermal tissues, and it is characterized clinically by mental retardation, convulsive attacks, and so-called sebaceous adenomas. A case has been reported which shows that the characteristic sclerotic areas in the cerebrum and within the cerebral ventricles may be demonstrated by roentgenography and encephalography.

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# PEDIATRIC DIAGNOSIS

WILBURT C. DAVISON, M.D.
DURHAM, N. C.

FREQUENTLY it is said, and perhaps with truth, that physicians today are not as keen diagnosticians as were those of the last generation. There are at least three possible reasons for this: (1) Most students have been taught by excellent older clinicians, who through long experience in quizzing patients and thumping chests, have learned to weigh essential symptoms and signs so quickly that they often seemed to make "snap diagnoses"; (2) with the crowding of the curriculum by additional courses in the newer specialties and in laboratory aids, there is a tendency to neglect fundamental training in history taking and physical diagnosis; and (3) many medical school courses in physical diagnosis are limited to percussion and auscultation of the thorax and do not include the diagnostic problems of the other portions of the body or an adequate consideration of children.[1] Students trained under the usual present methods emulate their preceptors and try to make similarly rapid diagnoses, which frequently are wrong. As a result, many young physicians spend more energy defending their "snap diagnoses" than would have been consumed in obtaining a careful history and doing a painstakingly accurate physical examination. There is no royal road to diagnosis; for every correct one made by quick impressions, there are a dozen which can be obtained only after a careful study of the information obtained by the methods shown in Table I.

TABLE I

METHODS OF EXAMINATION

| METHODS | DIAGNOSIS |
|---|---|
| History | Pain and its location; diet |
| Inspection | General diseases |
| Palpation | Surgical diseases |
| Percussion | Chest diseases |
| Auscultation | Chest diseases |
| Laboratory tests | Infectious and metabolic diseases |

A wealth of information can be collected by the careful application of these methods. One hundred fifty-nine different symptoms and signs can be elicited by a careful history and physical examination, and the results of the laboratory tests indicated in Table II will supply additional helpful knowledge. Certain of these tests should be done rou-

From the Department of Pediatrics, Duke University School of Medicine, and Duke Hospital, Durham, N. C.

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tinely. A Wassermann test should be performed on every child examined, regardless of clinical or social condition, and not alone on those children suspected of having syphilis. Certainly for every case of syphilis in children diagnosed by clinical signs, five are discovered by routine Wassermann tests. An intradermal tuberculin test which is negative will, with rare exceptions, eliminate the possibility of tuberculosis, while, if it is positive, an x-ray film usually will demonstrate whether the disease process is active or quiescent.[2]

These data often must be studied and restudied like clues in a detective story, for, after all, symptoms and signs are clues which may be caused by several diseases, all but one of which must be eliminated by the further study of the patient's other symptoms and often by the use of laboratory methods. For example, ten different symptoms and signs,

TABLE II

LABORATORY TESTS

| LABORATORY TESTS | DIAGNOSIS |
|---|---|
| *Routine tests* | |
| Tuberculin | Tuberculosis |
| Wassermann | Syphilis |
| Urinalysis | Nephritis, pyuria, diabetes |
| Hemoglobin | Anemia |
| Blood smear | Leucemia, purpura |
| *Special tests* | |
| Xray | Chest diseases, fractures |
| Blood chemistry | Metabolic diseases |
| Blood cultures | Systemic infections |
| Throat cultures and smears | Stomatitis, diphtheria |
| Stool cultures and smears | Dysentery, typhoid fever, parasites |
| Urine cultures | Pyuria, typhoid fever |
| Vaginal smears and hanging drop preparations | Gonorrhea, trichomonas vaginitis |

which may be caused by any one of one hundred and thirteen different pediatric diseases, can be detected by a careful inspection of the patient, and eight signs, caused by eighty-eight diseases, can be elicited by palpation, percussion, etc. A cross-reference table like a road map mileage chart would be ideal, but it is impractical; three of us tried arranging the one hundred fifty-nine pediatric symptoms and signs and the sixty-five laboratory tests into tables to facilitate the diagnosis of the three hundred seven diseases of children, but, except in a very limited way, the results usually were of no assistance. A similar attempt has been made to use this comparative method in adult diagnosis.[3] Clinical diagnosis, in the absence of specific tests, is an estimation, often subconscious, of probabilities, based upon experience, and any tabulation of the relative frequency of symptoms and signs must be corrected by judgment and observation.[4] This judgment and observation, of course, can be obtained only by experience, but, if a physician is assiduous in eliciting a wealth of symptoms and signs, these other attributes to diagnostic

ability eventually will be added unto him. The difficulty, of course, is remembering all or most of the diseases which may cause that particular symptom. For instance, ninety-five different conditions may produce vomiting in children, and any one of seventy-six diseases may be responsible for abdominal pain.[5] A printed "ready reminder" list of them should be available for consultation, not with the idea of making a cross-reference differential diagnosis, but merely as a list of possibilities which should not be overlooked. If a physician's mind were sufficiently "encyclopedic" to remember all of these possibilities without a reminder, the chances are that his brain would not be adequately analytical to utilize this information in making a diagnosis. A book or list can jog the memory on possibilities, but it cannot do a physician's thinking for him.

Obviously a discussion of all of these symptoms and signs is impractical here, so eight have been selected as examples. *Headaches* in children may be caused by sixty-seven diseases or conditions. To consider the complete differential diagnosis of all of them in arriving at a decision probably is absurd, but, if a physician before making a final diagnosis in a child who complains of headaches will at least read the list, he often will save himself and the patient much embarrassment and occasionally will correct an erroneous "snap diagnosis." As a rule, a student or physician notices the patient's most obvious symptoms and recalls that they occur in a certain disease, but frequently he forgets that these same symptoms may be present in several diseases. An erroneous diagnosis often is the result. For instance, if the patient has a headache, is nauseated, is mentally dull, and has fever, the student or physician may think of typhoid fever and not remember that these same symptoms also are characteristic of meningococcus meningitis. Obviously if the patient has meningitis, his chances of recovery are not increased by a delayed diagnosis, for they depend upon prompt recognition and vigorous serum therapy. A list serves as a ready reminder of easily forgotten possibilities, which if they are at least recalled to memory can be confirmed or eliminated by searching for additional symptoms and signs or by various laboratory procedures.

Children are too often sentenced to weeks or months in bed because a physician or a school nurse has heard a *cardiac murmur*. The majority of rapidly growing children have definitely audible heart murmurs, but true cardiac disease, both congenital and acquired, occurs in less than 2 per cent of them.[6] Obviously a glance at Table III may suggest to a physician the need of additional study of the patient's other symptoms before condemning the child to bed and completely demoralizing the family. Many pediatric and parental neuroses are caused by hasty and erroneous diagnosis of heart disease. Cardiac murmurs, of course, are of some importance but not nearly so much as are the measurement of heart size, the cardiac functional capacity, symptoms of decompensa-

tion, x-ray pictures of the chest, blood pressure determinations, electrocardiograms, and last but not least the effect of respiration on the murmur, as most functional murmurs disappear at the height of full inspiration. The cardiac size usually is increased if the murmur is due to heart disease. The murmur of any individual's heart generally can be correctly diagnosed if the physician will study a list such as Table III so that he will be reminded of several possibilities and then carefully weigh *all* of the factors concerned.

TABLE III

HEART MURMURS

| LOCATION | TIME | DIAGNOSIS |
|---|---|---|
| Apex | Systole | Functional |
| Apex | Systole | Mitral insufficiency |
| Apex | Diastole | Functional |
| Apex | Diastole | Mitral stenosis |
| Base | Systole | Functional |
| Base | Systole | Pulmonary stenosis |
| Base | Systole | Aortic stenosis |
| Base | Diastole | Aortic insufficiency |
| Base | Continuous | Patent ductus |
| Sternum | Systole | Patent septum |
| Sternum | Systole | Tricuspid insufficiency |

*Albuminuria* is another symptom which to some physicians suggests only "Bright's disease" with a grave prognosis. That conditions other than nephritis cause albuminuria can be seen in Table IV. Occasionally it is very embarrassing to see a child who has nothing but orthostatic albuminuria yet has been kept in bed for months on an erroneous diagnosis of nephritis. Because the physician had not considered orthostatic albuminuria, he had not compared day and night urine specimens and had not found that the night specimen was free of albumin. The parents, of course, must be told that the child is well and except for the

TABLE IV

CAUSES OF ALBUMINURIA[1]

| CONDITION | ESTIMATED CASE DISTRIBUTION (IN PER CENT) |
|---|---|
| Glomerular nephritis (acute, subacute and chronic hemorrhagic, exudative, purpuric) | 59 |
| Orthostatic albuminuria (lordotic) | 20 |
| Pyuria (pyelitis, pyelonephritis) | 16 |
| Tubular nephritis (acute and chronic nephrosis) | 3 |
| Interstitial nephritis (chronic nephritis with infantilism) | 1 |
| Paroxysmal hemoglobinuria | 1 |

need of corrective exercises and physiotherapy to remove his lordosis, he can attend school and play as other children. However, when they ask the reason for this sudden change of instructions from complete

bed rest to freedom from restraint, should they be informed that their former physician cured his patient or that because he did not consider all of the possible causes of albuminuria, he was mistaken in his diagnosis and that the child need not have been invalided? That question is raised too frequently to be amusing. After orthostatic albuminuria has been eliminated, the differentiation of the other forms of albuminuria is not difficult: red blood cells in the urine indicate glomerular damage; the presence of pus cells in clumps in the urine is diagnostic of pyuria; albuminuria with edema but without hematuria is characteristic of tubular nephritis, etc.

*Convulsions* occur in many childhood conditions, but a lumbar puncture, which should be performed on every child who has neurologic symptoms, and a glance at Table V frequently will suggest a tentative diagnosis which, of course, must be confirmed or eliminated by further study. If the patient has *meningitis*, the earlier adequate serotherapy is started, the better are the results.

TABLE V

SPINAL FLUID EXAMINATION

| APPEARANCE | CELL COUNT | ORGANISM | DIAGNOSIS |
|---|---|---|---|
| | | Acid-fast bacilli | Tuberculous meningitis (33%)* |
| Clear | 10-1,000 | None | Meningismus<br>Poliomyelitis<br>Encephalitis (lead, lethargic, etc.)<br>Mumps or syphilitic meningitis<br>Brain abscess or tumor |
| Turbid | 1,000-5,000 | Gram-negative cocci | Meningococcus meningitis (30%) |
| | | Gram-negative bacilli | Influenzal meningitis (13%)<br>Brucella meningitis |
| | | Gram-positive cocci | Pneumococcus meningitis (12%)<br>Streptococcus meningitis (7%)<br>Staphylococcus meningitis (0.5%) |

*Figure in parentheses indicates percentage of cases in children under two years of age due to that particular organism.[5]

Thus far, this discussion has been limited to the use of tables and lists as reminders of all of the diseases which may cause a particular symptom, but occasionally the tabular listing and comparison of all of the patient's symptoms and signs may lead to a diagnosis. For example, the differentiation of the several causes of *ataxia*, which after all is only a symptom and not a disease entity, is greatly facilitated if some such aid is used. A complete history and a careful physical examination are necessary, and clinical judgment, of course, is needed to evaluate the various symptoms and signs; but, unless all of them are compared, an erroneous diagnosis is frequent. When the proper technic is patiently pursued, the diagnosis usually makes itself.

The same observations apply to *muscular weakness* and the *myopathies*. Weakness is a common complaint, and "snap diagnoses" often

can be exceedingly harmful to the patient. Bed rest and diet instead of "building-up exercises" are needed if the child has tuberculosis, and psychiatric care and a change of environment, if the child is neurotic. Even a casual study and tabulation of the patient's other symptoms may suggest some forgotten possibility.

Finally, it is important to divide the 307 pediatric diseases into the 83 which are curable and the 224 from which the patients usually recover or succumb regardless of therapy.[5] Accurate and prompt diagnosis should be stressed in the first group and the latter diseases should not be considered until all possibility of the presence of one of the curable conditions is eliminated.

## CONCLUSIONS

1. A careful history and a complete physical examination always are necessary before even a tentative diagnosis is attempted.

2. All of the information available and every indication for further studies should be intelligently considered before a diagnosis can be established.

3. Symptoms and signs are clues which may be caused by several diseases, all but one of which must be eliminated by further study of the patient's other symptoms, and often by laboratory methods, before the correct diagnosis can be made.

4. "Snap" and often erroneous diagnoses can be avoided by a study of lists of all of the diseases which cause any particular symptom.

5. The presence or absence of a curable disease should be decided before considering the possibility of conditions for which adequate therapy is not available.

6. The art of arriving at a correct diagnosis is, or should be, based upon at least three processes: (a) remembering to obtain as many bits of evidence as possible, (b) recalling as many conditions as possible which will cause these symptoms, and (c) evaluating this material.

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# OMPHALITIS IN THE NEWBORN

JOHN W. CHAMBERLAIN, M.D.
BOSTON, MASS.

## INTRODUCTION

INFECTION of the umbilicus in the newborn was one of the most important causes of death among infants before the days of asepsis. Cullen[1] writes, "Until the advent of asepsis, myriads of children succumbed to umbilical infection within a few days or a few weeks after birth." Today the disease is seen frequently enough and is of sufficient import to warrant more attention than has been paid it in recent literature.

During the last half of the nineteenth century, there appeared several reports of epidemics of "erysipelas" and "gangrene" of the umbilicus. These were summarized by Audion[2] (1901) in an excellent paper and more recently have been reviewed in detail by Cullen. It was recognized that there was some relationship between puerperal fever and umbilical infection, and between the latter and the secondary lesions which make it so serious; it was not until the work of Pasteur and Lister that this relationship was understood. In spite of this understanding and the aseptic and antiseptic precautions taken at the time of delivery and for the first two or three weeks thereafter, umbilical infections still occur. In certain communities, parts of China for instance, where street dust is used as dusting powder for the cord, it is estimated (Reed)* that 50 per cent of newborn infants die of umbilical infection even today. In more civilized communities the incidence of fatal sequelae in the cases that do occur is sufficiently great to merit serious consideration of the disease by obstetrician, pediatrician, and surgeon.

## ANATOMY

Most of the pathology of the umbilicus, other than infection, is directly related to the embryology of the region and is a manifestation of arrested or abnormal development. Infection and its sequelae, on the other hand, are directly related to the normal anatomy and the physiologic changes taking place at the time of delivery and directly thereafter.

Up to the moment the cord is clamped or tied, the infant's blood is circulating through the two umbilical arteries and the umbilical vein. It will be recalled that the former are continuous at the umbilicus with the hypogastric arteries which rise from the internal iliac arteries in the pelvis, course along the back of the anterior abdominal wall on either side of the bladder, and converge to meet each other at the umbilicus.

From the Surgical Service, Children's Hospital and the Infants' Hospital.
*Quoted from Rice.

The umbilical vein (really the left umbilical vein) enters the abdomen at the umbilicus and passes upward as the free margin of the falciform ligament of the liver to the under surface of the latter. Here it gives off several branches and then, at the transverse fissure, divides into two branches. The larger joins the portal vein and enters the right lobe of the liver; the smaller continues upward as the ductus venosus to empty into the inferior vena cava. The fact that both the hypogastric arteries and umbilical vein are separated from the abdominal cavity only by a layer of peritoneum and a thin irregular layer of areolar tissue is an important anatomic relationship. Thus benign-appearing omphalitis or hypogastric arteritis may, by extending only a very short distance, become a fatal peritonitis.

The cutaneous lymphatics of the umbilical region (Cuneo and Marcillini, 1901) drain downward and outward to both inguinal regions. Lymph vessels arising just above the umbilicus drain upward and outward to both pectoral regions. The deeper lymphatics communicate with those of the fascial sheaths at the various levels.

When the umbilical cord is tied and cut, circulation of blood through the umbilical veins is permanently interrupted. The arteries become obliterated and project as the lateral umbilical ligaments. The vein and ductus venosus become obliterated and persist as the ligamentum teres and ligamentum venosum, respectively.

The nature of the process of obliteration and the time consumed are also of considerable importance because of their bearing on the spread of infection. Obliteration of the lumen of the vessels probably begins with partial emptying of the lumen and corresponding collapse of the vessel wall. It continues with the formation of a clot, its organization, and especially with a gradual proliferation of the subintimal layer of the vessel wall. The time consumed in the process is usually stated to be about five days. Study of autopsy material at the Children's Hospital reveals that the time consumed is from twenty to fifty days.* In other words, a lumen containing unorganized blood clot may be demonstrated not only with the microscope but with the naked eye during this time (Fig. 1). Final transformation of the vessels into fibrous cords requires a much longer time. Direct spread of organisms from an infected umbilicus via the vessels to the blood stream is thus facilitated for a much longer time than usually thought possible.

While the vessels are being obliterated, the cord is drying and separating. At the junction of the cord with the umbilicus, the skin is reflected onto the cord for a variable distance. As the cord dries, the ring of skin becomes smaller, so that by the time the cord separates, the raw surface which would otherwise be present is covered with a thin layer of skin and scar tissue. Probably a small area of clean granulation tissue should not be considered abnormal. Should the cord, for some reason,

*Farber, S.: Personal communication.

separate prematurely there would be left a larger raw, granulating surface in which would be incorporated the practically open ends of the partially obliterated umbilical vessels.

## ETIOLOGY

Sepsis of the umbilical structures may be due to saprophytic or pathogenic organisms, or both. The liability to invasion of pathogenic organisms is increased by the presence of and reaction to saprophytic organisms since the latter delay separation of the cord and healing of the umbilical wound (Audion).

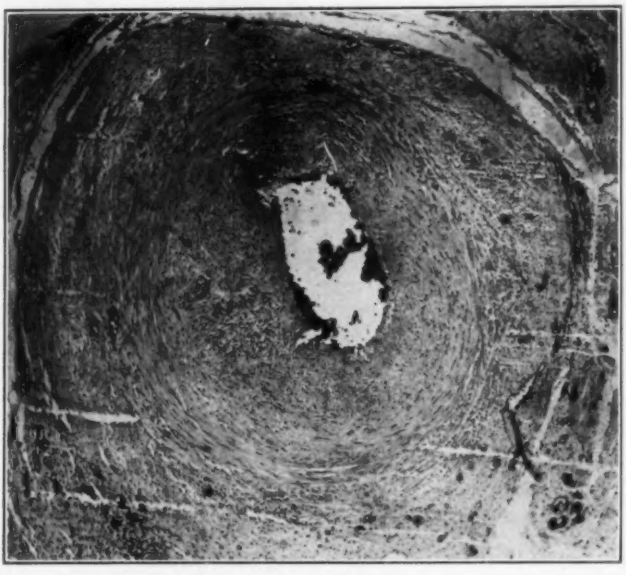

Fig. 1.—Low power (x60) photomicrograph of a hypogastric artery from a patient who died of dysentery and terminal bronchopneumonia at three and one-half weeks of age.

Bacterial invasion may occur intrapartum or postpartum. For many years it was thought that the birth canal did not contain pathogenic organisms, but it is now known that it frequently does. This is especially true when there have been frequent vaginal examinations during labor. It is not surprising, therefore, that Adair,[3] in a small series of cases, was able to recover pathogenic organisms from the surface of the cord and periumbilical region in 20 per cent of the cases studied. Premature rupture of the membranes and prolonged labor following this provides another route for intrapartum invasion with pathogenic organisms. Creadick[4] studied the umbilical cord in two thousand consecutive cases in which the infants weighed more than 1,800 gm. (4.2 pounds). Forty-three of these showed leucocytic infiltration (with polymorphonu-

clear and mononuclear cells) of the vessel walls and adjacent connective tissue. Usually the vein and sometimes the arteries were involved. Fourteen of these forty-three infants died, and in ten death was attributed to intrapartum infection.

Creadick pointed out that there were three possible sources of infection of the contents of the pregnant uterus: (1) by way of the maternal blood stream, (2) by way of the fallopian tubes, and (3) transamniotic, usually following premature rupture of the membranes. Sections through the insertion of the cord on the placenta showed branches of the umbilical vein involved in an inflammatory reaction in every one of the forty-three cases. In thirty-eight of these cases, the course of the reaction was traced backward into the subamniotic connective tissue. Premature rupture of the membranes occurred in twenty-six, and duration of labor was prolonged in twenty-five of the cases.

Siddall[5] more recently studied the association of inflammation of the umbilical cord with stillborn and premature infants. He found a much higher incidence of inflammation in the cords of these infants than in those delivered at term. In the cases he studied, however, the prognosis for the child was not affected by the presence of the inflammation.

While there may be an occasional case of fatal omphalitis due to intrapartum infection, by far the great majority of cases undoubtedly arise from postpartum contamination, from the scissors used to cut the cord, the material used to tie it, the hands of the doctor or nurse, or from the dressing.

*Streptococcus hemolyticus* and *Staphylococcus aureus* are the organisms most frequently recovered from the local lesion or blood stream. *Staphylococcus albus*, *B. coli* and pneumococcus are occasionally the infecting organism. In four hundred seven autopsies performed at the Hospital for Sick Children in Toronto (Wheeler),[6] there were nine cases of umbilical infection. *Streptococcus hemolyticus* was the infecting organism in four cases, *Staphylococcus aureus* in three cases, pneumococcus in one case, and *Streptococcus mucosus capsulatus* in one case.

## TYPES OF LESIONS

Infection of the umbilicus may manifest itself in a variety of ways depending on the nature of the infecting organism and the degree to which the umbilical and periumbilical structures are involved. For purposes of classification, Audion considered the cord, the umbilical wound or scar, and the umbilical vessels separately and in this way derived three catalogues of pathologic states:

1. Infection of the cord.
2. Infection of the umbilical wound.
   a. Blennorrhea, simple ulcer, granuloma.
   b. Fungus, malignant ulcer, gangrene, erysipelas, periumbilical lymphangitis.

3. Infection of the umbilical vessels.

It is obvious that one or several of the above pathologic states may be present in the same patient and that the most serious type of lesion may show the least or nothing at all on gross examination.

As far as ordinary gross examination is concerned, we need consider no more than four types of lesion: blennorrhea ("moist umbilicus"), phlegmon, ulcer, and infection of the umbilical vessels. The important thing to remember is that no matter what type of lesion appears to be present, it should be considered serious, and the prognosis should be guarded.

In the days of epidemic omphalitis, the local lesions were frequently very similar in character. In the sporadic cases now seen, the more benign lesions are similar, but the severe lesions vary markedly in appearance so that, just as there is no characteristic symptomatology, there is no one typical lesion.

By far the most frequently seen lesion is the benign-appearing, small, moist, granulating area in the middle of the umbilical wound with a slight mucoid or mucopurulent discharge. In the ten-year period covered by this report, one hundred forty-three cases were seen and treated in the Out-Patient Department of the Children's Hospital, usually with prompt healing. The more severe lesions are characterized by varying amounts of purulent discharge with or without palpable thickening of the hypogastric arteries and patency of the latter as demonstrated by probing, and by varying degrees of cellulitis and lymphangitis of the periumbilical tissues. In such cases, there is redness, swelling and induration which may remain localized or which may extend peripherally, particularly downward to the inguinal regions, thighs, and scrotum. A third, now infrequently seen, severe lesion is the malignant spreading ulcer with progressive discoloration, softening, and sloughing of tissue. This lesion may start at the umbilicus or may arise elsewhere on the anterior abdominal wall or chest wall due probably to migration of the infecting organisms from the umbilicus via the lymphatics.

In our experience the fatal cases have most often shown clinically a slight to moderate purulent discharge with or without evidence of slight periumbilical inflammation. Death has been due to blood stream invasion with consequent multiple metastatic lesions in bones, joints, and viscera, or to peritonitis, arising from direct extension of the umbilical infection.

## SYMPTOMATOLOGY

In concluding his discussion of umbilical infection in the newborn, Cullen (1916) states, "In every instance of illness in a newborn infant it should be the rule to inspect and, if necessary, reinspect the navel." This statement suggests the lack of specificity of the presenting symptoms. It is difficult to draw the line between mild out-patient department cases and house cases. It is significant, however, that whereas in

the former the only complaint may be "moist navel" or failure of the umbilicus to heal, in the latter the complaints may seem at first wholly unrelated to the umbilicus. Usually, however, on direct questioning it will be learned that, in addition to the general symptoms, the infant's navel has never been completely healed or that it has been discharging pus for a varying length of time.

The general symptoms depend, of course, on the nature and site of the secondary lesions. In fatal cases, there is usually a septicemia; this may result in multiple soft tissue abscess formation, multiple osteomyelitis, brain abscess, pneumonia, empyema, and other metastatic lesions. Frequently there is a peritonitis. Symptoms and signs will vary accordingly. In the nine cases reported by Wheeler, five had peritonitis, two had septicemia without localized lesions, one had multiple abscess formation, and one had thrombosis of the hypogastric and iliac arteries and abdominal aorta.

### TREATMENT

The treatment of omphalitis consists in cleansing the umbilical regions with soap and alcohol and in the repeated local application of wet dressings, usually of boric acid, hexylresorcinol, or magnesium sulphate solution. Occasionally alcohol dressings are used. Redundant granulation tissue is touched with silver nitrate. In the great majority of cases, this simple treatment results in rapid clearing up of the infection and complete healing of the umbilicus.

If there is extension of the infection into the hypogastric arteries with demonstrable abscess formation, incision and drainage is done, as there is rarely adequate drainage through the open end of these vessels. Pressure over the abscess will usually result in the appearance of a small amount of pus somewhere in the umbilical depression. At this point a probe and then a grooved director are inserted and passed downward into the abscess cavity. With the director as a guide, the abscess is then incised from above downward. Use of the grooved director is an essential precaution because of the proximity of the peritoneal cavity.

Treatment of the secondary or metastatic lesions is symptomatic and supportive. Abscesses are poulticed, incised, and drained as they develop; cellulitis is treated with cold magnesium sulphate compresses; and the spreading ulcers with wet dressings, heliotherapy and débridement. Parenteral fluids and blood transfusions are given when indicated.

There are far too many infants who arrive at the hospital too late to respond to any sort of treatment. These are the infants with blood stream infection and peritonitis, meningitis, or multiple abscesses, who get progressively worse and die within two or three to thirty-six hours after entry.

That the most promising treatment of omphalitis is prophylactic it is scarcely necessary to mention. Yet it is largely to point out the serious

consequences of carelessness in tying, cutting, and dressing the umbilical cord that this paper is written.

## SUMMARY OF CASES

During the ten-year period 1925 to 1934, inclusive, 74 patients with omphalitis were admitted to the wards of the Children's and the Infants' Hospitals. In 23 instances the omphalitis was incidental and not the primary reason for the hospitalization of the patient. It cleared up rapidly in those patients who did not die of other causes. In one of four fatal cases of intracranial hemorrhage with incidental omphalitis, there was postmortem evidence of an acute hypogastric arteritis, and in a fatal case of agranulocytosis there was terminal peritonitis which may have been secondary to the omphalitis; microscopic examination revealed a bilateral hypogastric arteritis.

Of the remaining 51 patients, 30 were males and 21 females. Thirty-three died, a mortality rate of 65 per cent. It should be pointed out that this is not the mortality rate of omphalitis, but rather of those cases in which the severity of the omphalitis or secondary lesions made admission to the hospital advisable. Various organisms were recovered from either the blood stream, umbilical discharge, or abscesses in 26 of the fatal and 12 of the nonfatal cases (Table I). It is noteworthy that *Streptococcus hemolyticus* alone was the infecting agent in 15 of the 26 fatal cases in which the organism was known and that either *Streptococcus hemolyticus* or *Staphylococcus aureus*, or both, were involved in all but 4 of these 26 fatal cases.

TABLE I

| ORGANISM | FATAL CASES | NONFATAL CASES | TOTAL |
|---|---|---|---|
| *Streptococcus hemolyticus* | 15 | 4 | 19 |
| *Staphylococcus aureus* | 5 | 5 | 10 |
| *Streptococcus hemolyticus* and *Staphylococcus aureus* | 2 | 1 | 3 |
| *Staphylococcus aureus* and *B. coli* | 1 | 1 | 2 |
| Pneumococcus | 1 | 1 | 1 |
| *Staphylococcus albus* | 0 | 1 | 1 |
| Pneumococcus and Flexner bacillus | 1 | 0 | 1 |
| *Staphylococcus aureus, Streptococcus viridans* and *B. coli* | 1 | 0 | 1 |
| Unknown | 7 | 6 | 13 |
| Totals | 33 | 18 | 51 |

The ages of the patients on admission varied considerably, the majority being between one and three weeks (Table II). It is a point of interest that all of 9 patients who were admitted to the Infants' Hospital between the fifteenth and twenty-first days of age and 6 of the 8 admitted to the Children's Hospital in the same age period died.

As might be expected, the most common complaint and positive finding was a purulent discharge or crusting of the umbilicus. This was

TABLE II

| AGES | FATAL CASES | NONFATAL CASES | TOTAL |
|---|---|---|---|
| 1 to 3 weeks | 24 | 9 | 33 |
| Less than 1 week | 3 | 3 | 6 |
| More than 3 weeks | 6 | 6 | 12 |
| Totals | 33 | 18 | 51 |

noted in 34 patients. In 25 instances there was redness and swelling of the umbilicus, 15 with purulent discharge. Cyanosis was noted or complained of on entry in 10 of the Infants' Hospital cases; 5 of them were premature infants. There were 15 cases with soft tissue abscesses, usually with other more serious lesions such as meningitis, peritonitis, or multiple osteomyelitis. A common complaint and finding was a tensely swollen and tympanitic abdomen. This usually indicated peritonitis, of which there were 15 cases. It was the most frequent complication and was invariably fatal. Cellulitis or erysipelas of the anterior abdominal wall was the next most frequent complication, occurring in 12 patients. In 8 instances the process extended to the external genitals. There were only 3 cases of osteomyelitis and 2 cases of extensive ulcer. One or both hypogastries were incised and drained in 4 infants, two of whom recovered. Evidence of hemorrhagic disease of the newborn was noted in 3 instances before the onset of the omphalitis, and in 2 of these cases the cord was retied one or more times.

The course of the disease process in the fatal cases varied considerably, but in the cases of peritonitis especially, it was very rapid, about half of these patients dying within twenty-four hours after entry.

The importance of examining the umbilicus carefully in any infant with an unexplained septic process is brought out by the fact that in 4 of the above fatal cases, the omphalitis, or source of infection from which the patient died, was unsuspected clinically.

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# THE INFLUENCE OF BREAST AND ARTIFICIAL FEEDING ON INFANTILE ECZEMA

CLIFFORD G. GRULEE, M.D., AND HEYWORTH N. SANFORD, M.D.
CHICAGO, ILL.

THERE is probably no subject in pediatrics that has received so much attention in the last few years as that of infantile eczema. Both external and internal factors have been studied, and some advances have been made in its treatment. We believe, however, that the effect of diet on these infants, once so stressed, has been largely lost sight of recently. For this reason the following study was made.

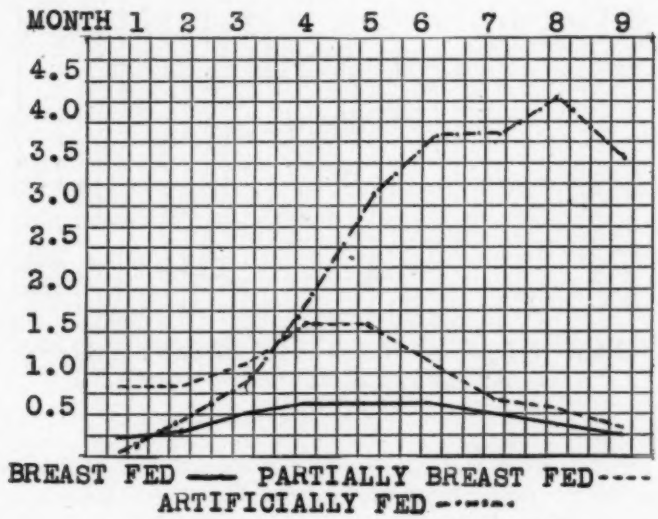


Chart 1.—Monthly incidence of infantile eczema.

The clinical material from which this study was made has been previously discussed.[1] The 20,061 babies represented in this study represent a five-year period in which each infant was fully followed.

An infant was considered as suffering from infantile eczema if there were any lesions on the face or body at the time of examination. This does not include "cradle cap." None of these infants received any treatment except the discontinuance of soap and water to the skin and the use of olive oil only for cleansing purposes. None of the feedings were changed in any way. In the artificially fed infants, 1.5 ounces of

From the Department of Pediatrics Rush Medical College, and the Infant Welfare Society of Chicago.

boiled cow's milk and 0.1 ounce of cane sugar per pound body weight were used. In all infants cod liver oil, orange juice, cereals, and vegetables were added to the diet.

In the total number of cases recorded, there were twice as many babies with infantile eczema in the partially breast-fed group as in the breast-fed group and seven times as many in the artificially fed group as in the breast-fed group. Another interesting fact is that, while in all groups the numbers are almost the same for the first three months, thereafter there is a rapid increase in the artificially fed group without any particular decrease at the end of the nine-month period; on the other hand, in both the completely breast-fed infants and the partially breast-fed infants the incidence of infantile eczema increases until the sixth month and then decreases markedly through the ninth month.

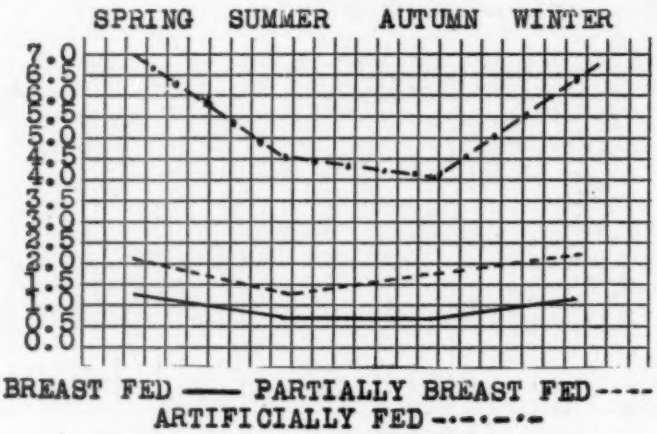


Chart 2.—Seasonal incidence of infantile eczema.

It may be argued that our feeding for the artificially fed babies is not an ideal one for the eczematous infant. This we will not deny. Our idea in the Infant Welfare Society is to keep up the infant's nutrition in spite of the effect it may have on the skin. In any case our greatest incidence in any month (the eighth) in the artificially fed babies was less than one in twenty (4.6 per cent), which we believe compares quite favorably with the usual incidence in private practice.

In the comparison of the seasonal incidence, the same proportion is shown. As to the general seasonal incidence, nothing new is added. In all groups the incidence is greatest in the spring and winter and lowest in the summer and autumn.

## CONCLUSIONS

The general incidence of infantile eczema is lowest in the breast-fed infants. In the partially breast-fed it is twice as frequent as in the

breast-fed infants and in the artificially fed infants, seven times as great.

In the monthly incidence both those infants entirely breast-fed and those partially breast fed show an increase to the sixth month and then a rapid decrease through the ninth month. The artificially fed infants

## RESULTS

TABLE I.

AGE IN MONTHS

| MONTH | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|---|
| *Breast-fed infants (number) | 1 | 9 | 47 | 60 | 63 | 63 | 43 | 27 | 18 |
| Percentage | 0 | 0.1 | 0.5 | 0.7 | 0.7 | 0.7 | 0.5 | 0.3 | 0.2 |
| Partially breast-fed infants (number) | 7 | 74 | 96 | 106 | 109 | 100 | 73 | 54 | 40 |
| Percentage | 0.8 | 0.8 | 1.1 | 1.7 | 1.7 | 1.1 | 0.8 | 0.6 | 0.4 |
| Artificially fed infants (number) | 0 | 8 | 14 | 30 | 54 | 71 | 71 | 79 | 61 |
| Percentage | 0.0 | 0.4 | 0.8 | 1.7 | 3.2 | 4.2 | 4.2 | 4.6 | 3.5 |

*The total number of breast-fed infants in this series was 9,749; the partially breast-fed, 8,605; and the artificially fed, 1,707.

TABLE II.

SEASONAL INCIDENCE

| | SPRING | SUMMER | AUTUMN | WINTER |
|---|---|---|---|---|
| Breast-fed infants (number) | 113 | 60 | 59 | 99 |
| Percentage | 1.3 | 0.8 | 0.7 | 1.1 |
| Partially breast-fed infants (number) | 187 | 126 | 149 | 197 |
| Percentage | 2.1 | 1.4 | 1.7 | 2.3 |
| Artificially fed infants (number) | 122 | 78 | 72 | 116 |
| Percentage | 7.0 | 4.6 | 4.2 | 6.8 |

continue to show an increase until the eighth month and only a slight decline in the ninth month.

In the seasonal incidence all groups are increased in the winter and spring and decreased in the summer and autumn.

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636 CHURCH STREET, EVANSTON, ILL.
952 NORTH MICHIGAN AVENUE, CHICAGO.

# A CAPILLARY RESISTANCE TEST AND ITS RELATION TO VITAMINS C AND D

C. B. WELD, M.D.
TORONTO, ONTARIO

NO precise method is yet established by which we can determine the optimal amounts of vitamin C required by humans. In a rough way the amounts necessary to prevent actual scurvy from developing are known, but, even if enough be present to prevent scurvy, it is possible that there may be insufficient to preserve optimal health conditions.

Among the various manifestations of scurvy the hemorrhagic tendency has been suggested as that most useful for detecting latent or subclinical cases. The hemorrhages are due to an increased permeability of capillaries, and several workers have suggested the use of the capillary resistance test to diagnose latent scurvy. For example, Hess and Fish[3] in 1914 developed the method of Rumpel[1] (1909), and Leede in 1911, reported that *most* cases of scurvy were positive but emphasized that the test was not specific for scurvy. In 1930 Göthlin[4] of Sweden standardized a technic and applied it to a large number of Swedish school children and adults. He established normal standards and concluded that 18 per cent of the school children were undernourished in regard to vitamin C. His method, however, may take half an hour or more to perform and is so uncomfortable to the subject that it is difficult to apply to young children. In 1907 Hecht[5] suggested a simpler method, involving the use of a suction cup instead of venous congestion as a means of putting stress upon the capillaries. Da Silva Mello used it in 1929, and in 1933 Dalldorf[6] used this method in a survey of 250 convalescent hospital patients who were receiving an excellent diet and of 50 adult and 50 children members of families in poor circumstances. These family groups were shown to have a somewhat lower capillary resistance than the hospital group. The capillary fragility of the children improved after admission to a preventorium. He has also reported prompt improvement of capillary resistance following administration of ascorbic (cevitamic) acid.

We hoped that some such method might be useful to us in detecting early or mild cases of vitamin C deficiency, and hence be of service in determining the optimal vitamin C content of the diet. We first applied Dalldorf's technic (in which the lowest degree of suction necessary to produce any petechiae, in a cup 1 cm. in diameter applied to the skin

From the wards and laboratories of the Hospital for Sick Children and the Department of Paediatrics, University of Toronto, under the direction of Alan Brown, M.D., F.R.C.P.(C.).

of the outer aspect of the upper arm for one minute, determines the threshold) to a group of normal individuals. This consisted of members of the laboratory staff, and convalescent cases in the hospital. The ages of the children ranged from four to fourteen years, the infants being under two years of age. All were receiving adequate amounts of vitamin C in the diet. In the cases of the infants the skin of the abdomen was used instead of that of the upper arm, though in several instances the arms were tested as well, with similar results. The results are given in Table I, from which it will be seen that in the cases of the children and adult groups much variation in the threshold of capillary resistance is found.

TABLE I

| NORMAL SUBJECTS | | | |
|---|---|---|---|
| THRESHOLD AT WHICH PETECHIAE ARE PRODUCED (CM. HG) | INFANTS NUMBER OF SUBJECTS | CHILDREN NUMBER | ADULTS NUMBER |
| Over 50 | 18 | 23 | 9 |
| 50-40 | 6 | 22 | 7 |
| 35-25 | – | 12 | 4 |
| 20-15 | – | 6 | 2 |
| 10 | – | – | 1 |

Of the 85 children and adult subjects, 32 gave no petechiae even at 50 cm. of mercury suction, but the thresholds of 23 were 35 cm. of mercury or below and of these, 9 gave petechiae at 20 cm. of mercury or less. Of the 24 infants, however, only 6 gave any petechiae at 40 cm. of mercury suction, and none at lower levels. One would conclude, therefore, that infants show a greater capillary resistance than older children or adults.

Permission was granted by the Provincial Department of Health to determine the capillary resistances of a group of adult patients in a hospital, both on the ordinary hospital regimen and after supplementing their diet with tomato juice. These subjects were all fairly normal physically and were all receiving the same diet which is low in vitamin C. The group therefore should be particularly suitable for a survey of this type. A typical day's ration was as follows:

Breakfast: Cereal with milk and sugar; bread, butter and jam; coffee and milk (pasteurized).

Dinner: Split pea soup; meat pie, turnips and potatoes; bread; sago pudding, tea and milk.

Supper: Vegetable soup; bread and butter; preserved rhubarb and cake; tea and milk.

The only constant source of vitamin C is the daily portion of potato. The other vegetable in the instance given (turnip) would also be a source, but this vegetable is not a daily portion. About twice a week a cabbage salad is included in the menu for one meal.

Two groups of such subjects have been investigated. To the first, in the winter of 1934, each man was given 2 ounces of tomato juice daily for one week as supplement to the diet between capillary resistance estimations. In the second investigation a different group, conducted in the summer of 1935, each man was given 4 ounces of tomato juice daily for nearly three weeks. The larger dosage of tomato juice was given to meet the criticism that possibly in the first series an insufficient amount had been given. The tomato juice was found by analysis to contain an average of 17 mg. ascorbic acid per 100 c.c. During the summer the institutional diet contained perhaps three salads a week instead of the previous two, but fresh fruits were rarely given, and the diet would still be considered low in vitamin C. However, during the three weeks of tomato juice administration to this summer series, fresh tomatoes flooded the market, and the patients were given them freely. More than the 4 ounces of tomato juice calculated upon was therefore given; but, as this should merely accentuate any differences found in the capillary resistances, the conclusions are strengthened and not invalidated.

The results of these series are given in Table II in which the distribution of the subjects according to their threshold of capillary resistance is shown.

TABLE II

| THRESHOLD AT WHICH PETECHIAE ARE PRODUCED (CM. HG) | NUMBER OF SUBJECTS | | | |
|---|---|---|---|---|
| | WINTER SERIES | | SUMMER SERIES | |
| | BEFORE "C" | AFTER "C" 2 OZ. TOMATO JUICE DAILY FOR 1 WK. | BEFORE "C" | AFTER "C" 4 OZ. TOMATO JUICE DAILY FOR 3 WK. |
| Over 50 | 3 | 2 | 1 | 1 |
| 50-45 | 1 | 1 | 2 | 5 |
| 40-35 | 5 | 12 | 6 | 8 |
| 30-25 | 22 | 18 | 15 | 7 |
| 20-15 | 8 | 7 | 12 | 16 |
| 10 | 2 | 1 | 5 | 4 |
| Total | 41 | 41 | 41 | 41 |

It will be seen that the spread or distribution of the patients among the different threshold levels is not strikingly influenced by the added vitamin C. One would conclude indeed that the vitamin probably did not appreciably affect the capillary resistance. However, to further explore these results they have been arranged differently in Table III in which are recorded the numbers of subjects who showed a change in threshold following the administration of tomato juice.

It will be seen from these figures that of the winter series 11 subjects showed a greater capillary resistance after tomato juice while 9 showed lower capillary resistance, and the threshold of 21 was unchanged. Similarly, of the summer series, 13 showed an improved capillary resistance, but 11 showed a diminished resistance, and 17 showed no change.

TABLE III

| SERIES | CHANGE IN THRESHOLD BETWEEN TESTS | THRESHOLD AT FIRST TEST (CM. HG) | | | TOTAL SUBJECTS |
|---|---|---|---|---|---|
| | | OVER 50-40 | 35-25 | 20-10 | |
| Winter | Increase | 0 | 6 | 5 | 11 |
| | Unchanged | 6 | 10 | 5 | 21 |
| | Decrease | 3 | 6 | 0 | 9 |
| Summer | Increase | 3 | 5 | 5 | 13 |
| | Unchanged | 3 | 5 | 9 | 17 |
| | Decrease | 3 | 5 | 3 | 11 |

In this table, too, the possibility is explored that only those subjects showing a rather low capillary resistance might show an improvement following vitamin C administration. If the winter series alone is considered, suggestion of this is seen, but, after including the summer series which incidentally were given much more tomato juice, this result becomes much less striking. Little evidence, therefore, is given by the results shown in this table to suggest an improvement of capillary resistance consequent upon administration of vitamin C.

Through the courtesy of Dr. McHenry, of the School of Hygiene, University of Toronto, we have also been able to ascertain the ascorbic acid content of the urine (fasting specimens) of some of these patients on the days of the capillary resistance determinations. Twenty patients of the summer series were investigated in this way, and the results given

TABLE IV

CORRELATION BETWEEN ASCORBIC ACID CONTENT OF URINE AND CAPILLARY RESISTANCE (SUMMER SERIES)

| CASE | BEFORE "C" | | AFTER "C" | |
|---|---|---|---|---|
| | ASCORBIC ACID (MG. %) | THRESHOLD (CM. HG) | ASCORBIC ACID (MG. %) | THRESHOLD (CM. HG) |
| 1 | 0.5 | 50 | 0.3 | 40 |
| 2 | 0.6 | 30 | 1.0 | 30 |
| 3 | 0.7 | 25 | 1.1 | 20 |
| 4 | 0.7 | 30 | 0.9 | 35 |
| 5 | 0.8 | 25 | 1.2 | 35 |
| 6 | 0.9 | 20 | 1.9 | 30 |
| 7 | 1.0 | 40 | 0.9 | 25 |
| 8 | 1.0 | 20 | 0.9 | 20 |
| 9 | 1.1 | 30 | 1.4 | 40 |
| 10 | 1.1 | 20 | 0.8 | 20 |
| 11 | 1.1 | 20 | 0.7 | 10 |
| 12 | 1.2 | 10 | 1.1 | 25 |
| 13 | 1.3 | 20 | 1.4 | 20 |
| 14 | 1.3 | 50 | 1.9 | 50 |
| 15 | 1.4 | 10 | 0.7 | 20 |
| 16 | 1.5 | 25 | 1.3 | 30 |
| 17 | 1.5 | 30 | 1.3 | 20 |
| 18 | 1.5 | 20 | 1.3 | 10 |
| 19 | 1.7 | 25 | 1.4 | 25 |
| 20 | 2.1 | 40 | 1.3 | 40 |
| Average | 1.15 | 27.0 | 1.14 | 27.3 |

in Table IV in which the individual figures of the ascorbic acid content of the urine and the capillary resistance thresholds are placed side by side.

These results show no correlation whatever between the urine and capillary figures. Furthermore, the administration of tomato juice has had no effect upon these figures, the average ascorbic acid content of the urines and the average capillary resistance remaining unchanged.

While these investigations were being carried on we were fortunate in being able to observe ten infants with abnormally low vitamin C intake. Four of these were not scorbutic but had had no known source of vitamin C for two months or more; all four had a normal capillary resistance. The other six had scurvy, and in only one of these was the capillary resistance definitely low. Two were severe cases; one gave petechiae at the very low level of 3 cm. of mercury suction, while the threshold of the other was 40 cm. of mercury. The third was diagnosed on the basis of type of beading, x-ray findings, and history of no orange juice. The diet, however, was deficient in other ways as well, and the child was severely anemic and underweight. Orange juice promptly cleared up the irritability, during which time the capillary resistance threshold fell to 30 cm. of mercury. The fourth case was diagnosed on the basis of tenderness, beading, and x-ray, and was cleared up by the addition of orange juice to the diet, but the mother insisted that the child had always received the juice of an orange every day. The fifth case presented definite evidence of scurvy which, however, was showing x-ray evidence of healing (calcification of subperiosteal hemorrhages). Orange juice had been given prior to admission. The sixth case showed bleeding from the gums, slight scorbutic beading of ribs, tenderness about knees, and irritability, and was promptly cleared up with orange juice. The x-ray findings, however, were barely suggestive of scurvy.

It must be concluded therefore that in infants gross deficiency of vitamin C in the diet, even to the extent of scurvy development, does not necessarily result in a low capillary resistance. On the other hand, in adults a very low capillary resistance may be present even though ample amounts of vitamin C are being ingested. Since this paper was written, but before it was sent for publication, Abt and his coworkers[7] have reported a relation between diet and the reduced ascorbic acid content of the blood. They were, however, unable to correlate the vitamin C level of diet of the ascorbic acid level of the blood with the capillary resistances of their subjects. Hawley, Stephens and Anderson[8] have been unable to correlate the ascorbic acid content of the blood with the diet level of vitamin C, and they state that the capillary resistance does not parallel either of these factors.

During the course of these investigations, my own capillary resistance was found to be consistently low. As a final test before concluding that the dietary level of vitamin C had no relation to the capillary

resistance, I took an added 8 ounces of freshly expressed orange juice daily for six weeks without making any other change in my diet or mode of life. No change in the capillary resistance occurred, the threshold of suction at which petechiae were obtained remaining at 30 cm. of mercury. However, shortly after this I went on a summer vacation and on my return found that no petechiae could be elicited even at 50 cm. of mercury suction. This remarkable increase in the capillary resistance lasted for more than two months before returning to the original value. A similar improvement was noted twice during the autumn, each time following a golf game and persisting only a few days.

In view of these observations, it was decided to determine the effect of irradiation with a mercury arc quartz lamp and of administration of viosterol upon the capillary resistance. Eleven subjects whose resistance was low enough to be susceptible of improvement were irradiated

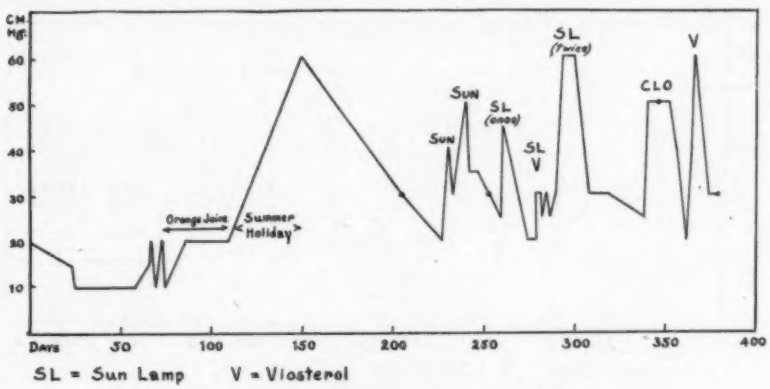


Fig. 1.—Capillary resistance thresholds.

or given viosterol for short periods of time. In three of the individuals observations could be made over a protracted period, and several courses of treatment were given. These individuals were laboratory workers, while the other subjects were convalescent children in the wards of the hospital, who were nearly ready for discharge. In all but one of the eleven subjects the irradiation and the viosterol treatments promptly resulted in a striking improvement in the capillary fragility, the improvement occurring usually within twenty-four hours. The dosage of viosterol given to the children was 10 drops daily for three or four days while in some instances rather larger doses were given to the adults. In no case were large enough doses given to make one think of overdosage effects. So far as the irradiation is concerned, the children were stripped except for a loin cloth and exposed prone and supine for 15 to 30 seconds in each position. This caused no glow or flushing to be apparent six hours after exposure. The adults were stripped to the waist only and

the dosage aimed at was just sufficient to cause a feeling of warmth to become perceptible six or eight hours after exposure, but to leave no traces whatever the next morning. There was never any burn produced.

The details and results of the three laboratory subjects will now be discussed. One of these is the only one of the eleven who failed to respond to viosterol or irradiation as did the others. Her very fair skin necessitated only short exposures to the lamp, and even so some desquamation resulted. In two of the three series of lamp treatments her capillary resistance was diminished, a brisk rise being noted on the other occasion. Her response to viosterol too was irregular, a doubtful improvement being noted on one occasion and a definite reduction on another. She failed to show an increased threshold with orange juice, eight ounces being given daily for a week. Another of these subjects was myself, the results being given in Fig. 1. The first part of the

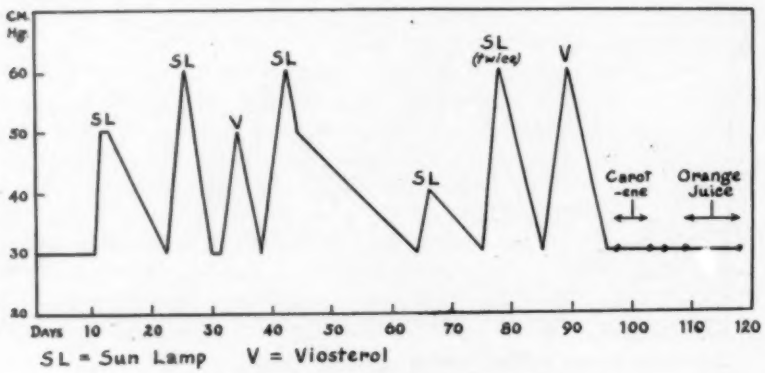


Fig. 2.—Capillary resistance thresholds.

curve has already been discussed, in which no response was obtained to orange juice, but a striking response was noted as a result of the summer holiday and the golf games. Equally definite improvements in capillary resistance occurred after sun lamp irradiation, after a single dose of 16 c.c. 10-D cod liver oil, and after 20 drops of viosterol daily over three days. The third of these subjects showed a remarkably consistent normal threshold at 30 cm. of mercury. His results are shown in Fig. 2. In all five instances in which he was irradiated he showed a striking rise in his threshold which then returned to its original level. Similar results followed the administration of viosterol, which was given twice, two doses of 10 drops each being given on the first occasion and three doses of 50 drops each on the second occasion. He failed to show any change in his capillary fragility to carotene or to orange juice administration. Eight ounces of orange juice were given daily for a week, and carotene equivalent to 40 c.c. cod liver oil was given in three doses.

In these results the striking feature is not only the response to the irradiation or viosterol but the return to the previous level and the repeatable nature of the observations. As each subject forms his own control, one is not depending upon statistical calculations to prove the point.

## SUMMARY

The capillary resistance method of Dalldorf has been applied to a number of normal individuals and a great variation in their responses found. Young children tend to have a higher resistance than older children or adults. No improvement in the capillary resistance following administration of tomato juice was observed in a group of eighty adults. These were in an institution, their diet was well controlled, and it was one low in vitamin C. Several children suffering from scurvy or known to have had no source of vitamin C for weeks were found to have normal resistances. In ten of eleven subjects viosterol in moderate doses or irradiation with an ultraviolet lamp promptly raised the capillary resistance.

## CONCLUSIONS

The capillary resistance determination is not a useful means of determining the state of nutrition with regard to vitamin C. Vitamin D is a more effective agent than vitamin C in increasing the capillary resistances.

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# RHEUMATIC INVOLVEMENT OF THE APPENDIX

ALEXANDER T. MARTIN, M.D., AND SAMUEL L. ELLENBERG, M.D.
NEW YORK, N. Y.

PHYSICIANS of our modern era are beginning to appreciate a fact which was well known and quite freely commented upon by the medical reporters of other days, namely, the widespread distribution of the rheumatic process and its many bizarre and devious symptoms and manifestations. The older literature abounds with illustrations of rheumatism involving practically every structure in the body with the peculiar result that succeeding writers, exasperated with this extreme point of view, shifted in the opposite direction and commented very little on this malady—leaving it for present-day writers to rediscover gradually and to call attention again to the various manifestations of this rheumatic state.

Within recent years, little comment has been aroused relative to the involvement of the heart, joints, brain, pleura, and blood vessels by the rheumatic virus, whereas involvement of the appendix and the peritoneum is still viewed with considerable skepticism by a good many modern writers. Present-day textbooks of medicine fail almost entirely to consider the possibility of a peritoneal invasion by rheumatic fever and are in complete accord on the invulnerability of the abdominal structures to the rheumatic virus.

Although as early as 1880 Lambin concluded that acute rheumatism can localize itself anywhere in the digestive tract, the clinical entity of rheumatic appendicitis has not been given very much credence. In 1930 Giraldi, after reviewing the literature on abdominal symptoms in rheumatism, concluded that "in some instances acute rheumatism may give rise to abdominal symptoms simulating appendicitis, but at present there is no warrant for the use of the term rheumatic appendicitis."

As late as 1934 Guptill in discussing the differential diagnosis of abdominal manifestations of acute rheumatic fever from acute appendicitis also felt that there was no gross or macroscopic evidence that rheumatic involvement of the appendix occurs. However, within recent years careful examination of pathologic material from rheumatic fever patients has resulted in a slow accumulation of evidence which indicates there may be definite rheumatic involvement in certain cases.

The following case is reported as illustrating the belief that rheumatic involvement of the appendix can take place.

A. B., a colored lad, aged eleven years, was admitted to the Children's Surgical Ward of Lincoln Hospital April 30, 1935, with a history of pain in the epigastrium, which had begun two days previously and later had radiated to

From the Pediatric Service of Lincoln Hospital.

the right lower quadrant where it persisted and remained localized. There was no accompanying nausea, vomiting, or diarrhea, no cough, no pain in the chest, but anorexia was present from the onset of symptoms. The past history did not reveal any previous attack, but the patient had had measles, mumps, and pertussis, and a tonsil and adenoid operation was performed a year ago at the hospital. Physical examination disclosed a well-developed and moderately nourished lad, not appearing very acutely ill, although he had a temperature of 102.4° F., pulse, 100; respiration, 26. His ears, nose, and throat were negative; lungs, clear. The heart was not enlarged, had a regular rhythm, sounds of good quality, no murmur; P 2 > A 2; his blood pressure was 140/85. The abdomen moved freely with respiration; there was no skin hyperesthesia. Spasticity, tenderness, and rebound tenderness were present in right lower quadrant, most marked over McBurney's point. Rectal examination showed tenderness on the right but no masses.

*Laboratory Findings.*—The urine was negative; white blood cells numbered 12,000; 70 per cent segmented and 26 per cent unsegmented polymorphs; 4 per cent lymphocytes; red blood cells, 4,900,000; Wassermann reaction, negative. The blood chemistry was normal. A diagnosis of acute appendicitis was made, and the patient was operated on shortly after. "An appendix 3 inches long with a serosal coat much injected was removed after being freed from some bands which bound it down. No free fluid was found in peritoneal cavity."

On the second day postoperative, patient began to run a temperature which varied between 103 and 104° F. The patient had no complaints; the abdomen was soft; and there was no apparent cause for the temperature—the urinalysis was essentially negative except for a very faint trace of albumin. On the seventh day postoperative patient still had a temperature, but he appeared comfortable; the throat was not injected; the lungs were clear; the abdomen was soft, there were no masses. Rectal examination showed slight tenderness on the right, and a systolic murmur appeared at the apex, but the heart rate and rhythm were regular. The white blood cells numbered 9,300; polymorphs, 84 per cent; lymphocytes, 13 per cent; monocytes, 3 per cent. The sedimentation rate was rapid, the blood settling 26 mm. in twenty minutes (modified Cutler method).

The following day a pediatric consultation was requested in view of the suspicion that the persistent postoperative temperature of 103 to 104° F., unaccounted for by anything in the abdomen, with a pulse rate from 90 to 110 and the development of a systolic murmur and a rapid sedimentation time plus a negative x-ray plate for a possible pneumonic focus, pointed to a rheumatic process. The pediatric service agreed in suspecting an abdominal manifestation of rheumatic fever and advised the use of salicylates as a therapeutic measure.

Of interest is the pathologic report which came back approximately at the time the belief that the patient was suffering from an unusual manifestation of rheumatic fever was gaining ground. Dr. Chester R. Brown, the pathologist, reported the following: "Specimen consists of an appendix measuring 6½ × 1 cm. with mild serosal injection present. *Microscopic.*—Slides reveal a peculiar hyalinization and a thickening of the serosa. Submucosal fibrosis is marked. The latter and the muscular layer, also, show peculiar areas of hyaline or fibrinoid degeneration. Submucosa infiltrated with lymphocytes and some plasma cells—no polynucleoses. Mucosa hyperplastic and hemorrhagic and presents marked lymphatic hyperplasia. Any evidence of rheumatism?"

The past history of the patient was now carefully checked for a history of any previous rheumatic episode or early rheumatic manifestation, but none was found. The family history was also essentially negative.

On May 11 the systolic murmur grew in intensity and was transmitted to the axilla while a short presystolic rumble also made its appearance at the apex. Examination of the heart on May 14 showed enlargement of the left border, a

marked sinus arrhythmia, a soft systolic murmur to the left of sternum with a rough systolic and diastolic murmur over the aortic area transmitted to the neck; no thrill or shocks were noted. Typical Corrigan pulse. Blood pressure was 134/48.

With the administration of salicylates the temperature promptly came down to normal, and the convalescence of the child was uneventful. The sedimentation rate continued to be rapid for a time, and then began to show some subsidence on June 16, 1935, and continued going down very gradually until the time of discharge on July 11, 1935. Electrocardiograms taken on May 28 and June 26 were essentially normal, while x-ray films of the heart showed slight enlargement of the cardiac shadow.

## DISCUSSION

The clinical course of this case coupled with the pathologic report makes one consider very seriously the clinical and pathologic entity of a rheumatic appendicitis. Graham and Paul[4] in 1926 pointed the way to a serious consideration of the possibility of the rheumatic involvement of peritoneal structures by their highly instructive postmortem study of eighteen cases of rheumatic fever in which they were able to demonstrate a definite inflammatory condition of the peritoneal structures in some of the cases.

In 1930 Paul[5] demonstrated through the postmortem study of a patient who had rheumatic polyarthritis, endocarditis, pericarditis, pleurisy, and pain in the right side that peritoneal lesions were present, closely resembling both grossly and histologically, coexistent pleural and pericardial lesions which were of a typical rheumatic nature.

In 1933 Coburn[6] offered a valuable contribution to the pathologic study of rheumatism. He demonstrated that during the initial cycle of a rheumatic attack, hemorrhagic lesions without distinctive histologic structure were prominent and that this cycle was also characterized by vasodilatation, swelling of the endothelium, necrosis of the collagen fibers, infiltration with various wandering cells, and the absence of detectable microorganisms. Included in his study were two cases of involvement of peritoneal structures. In one the vermiform appendix showed subserous hemorrhages; the subserosal vessels were slightly dilated in the distal half; and some clotted blood was attached to the serosal surface of the proximal half, while one or two small ecchymoses were seen in the submucosa. In the second case the appendix was found to be hemorrhagic and the histologic examination revealed a partially broken down blood clot in the lumen without evidence of inflammation; sections of the appendix showed the architecture replaced by fibrofatty tissue, and superimposed on this was an acute hemorrhagic picture with marked hemorrhagic exudate in the lumen.

Judging from the reports in the literature where there has been apparent involvement of the peritoneum or the appendix in rheumatic patients, it would seem that Coburn's observations are well founded since it is invariably mentioned, in those cases in which operation was performed for abdominal symptoms, that hyperemia, edema, and infiltra-

tion of the peritoneum and subperitoneal tissues and clear fluid were found while the appendix usually was edematous and injected, with a variable amount of inflammatory reaction.

Giraldi's[1] review of the literature on this subject reveals that the etiologic relationship between acute rheumatism and acute appendicitis was frequently commented upon by the older writers. Sir James Grant[7] in 1893 and I. Burney Yeo[8] in 1894 reported cases of appendicitis which they attributed to rheumatism. Haig[42] also reported several cases of perityphlitis which he regarded as rheumatic and gouty in nature and successfully treated them with salicylates. Of all the English writers, Sutherland[9] seemed most convinced of the rheumatic origin of appendicitis. Finney and Hamburger[10] reported three interesting cases as examples of the relationship between the two diseases. Moffett and Rodgers[11] described two cases in which they regarded the abdominal symptoms as part of the rheumatic infection, and not as a genuine appendicitis, and Grenet[12] was convinced that acute rheumatism may be ushered in by a pseudoappendicular syndrome. Kelly and Hurdon[13] concluded that clinical evidence is in favor of an intimate relation between appendicitis and acute rheumatism. Nothnagel[14] offered the interesting theory that some cases of appendicitis begin as a rheumatic inflammation and subsequently become infected with other microorganisms. However, in contrast to these opinions Giraldi quotes Edwards, Poynton, and Morris as not attaching importance to rheumatism as a cause of appendicitis.

From our knowledge of the fact that rheumatism has a predilection for the lymphoid tissues—as for example the frequent involvement of the tonsils—we ought not to be surprised if the appendix is involved. Bland Sutton[18] called the vermiform appendix the "tonsil of the abdomen" when discussing the anatomy of this vestigial structure, laying stress on its richness in lymphoid tissue.

It is to be admitted that the diagnosis of rheumatic appendicitis is a difficult one to make. Our case, in common with most of the cases reported in the literature, did not give any clue as to its possible rheumatic origin until about four or five days after the onset of symptoms, when the development of a carditis pointed to the etiologic factor. It has been noted by other authors that the abdominal symptoms are preceded or followed in a few days by arthritic or myocardial manifestations but are not coexistent with them.

Guptill[3] in discussing the differential diagnosis of abdominal manifestations of acute rheumatic fever from acute appendicitis offers the following helpful points: (1) vomiting is less frequent in rheumatism. (2) A history of sore throat coincident or directly preceding acute rheumatic fever is often elicited in 30 to 40 per cent of the cases. (3) In acute appendicitis muscular spasm corresponds in extent with abdominal tenderness. (4) Jesierski[43] has noted miosis of the left eye from pressure in the ileocecal region in appendicitis. (5) Livingston claims that in

86 per cent of the cases of acute appendicitis prior to perforation there is a definite triangle in the right lower quadrant of hypersensitiveness of the tissues of the abdominal wall to pinching. (6) Yaguda[20] reports a constant increase in the percentage of immature polymorphonuclear cells in appendicitis consistent with the degree of suppuration.

As will readily be understood, no absolute rule can be set up for the treatment of these cases. When abdominal symptoms referable to the appendiceal region develop in an individual who gives a history of rheumatism or presents evidence of an old rheumatic condition, or who is passing through an acute attack of rheumatic fever, it is the policy of wisdom to treat such a patient expectantly with salicylates. These ought to allay the symptoms promptly. If a therapeutic response is not obtained within twenty-four hours of the administration of salicylates, an appendectomy or exploratory laparotomy is in order, for the literature does record cases of suppurative appendicitis developing in patients already suffering from rheumatic fever, tonsillitis, or upper respiratory infections. In cases in which neither a history nor physical evidence of rheumatism is obtained and reasonable doubt is entertained as to the diagnosis, operative interference is the treatment of choice since the diagnosis of rheumatic appendicitis or peritonitis is still too uncertain at the present time to justify consideration of any treatment other than operation. Although the lesions found in most cases of rheumatic peritonitis or rheumatic involvement of the appendix may not be of a serious enough nature to justify surgical interference, nevertheless they are of value in focusing attention on the gastrointestinal tract as a possible source of information regarding the pathogenesis of rheumatic fever.

## CONCLUSIONS

1. A case is reported which helps to support the serious consideration of a rheumatic involvement of the appendix.

2. The pathology exhibited by the appendices removed from rheumatic individuals usually shows vasodilatation, necrosis of the collagen fibers, infiltration of various wandering cells and hemorrhages and, therefore, seems to correspond to the hemorrhagic lesions without distinctive histologic structure to which Coburn called attention as being predominant in the initial cycle of a rheumatic attack.

3. The diagnosis of rheumatic appendicitis is difficult to make at times but should be considered in any patient presenting signs and symptoms referable to the appendiceal region and giving a history of rheumatic fever or showing any of the manifestations of rheumatism.

4. The abdominal symptoms in rheumatism are usually followed in a few days by arthritic or cardiac manifestations but are not coexistent with them.

5. The treatment in an individual patient will depend upon whether a diagnosis of rheumatic involvement of the appendix can be made defi-

nitely. If this diagnosis is made, salicylates are indicated. If any doubt exists as to the diagnosis, or if the therapeutic response to salicylates is not obtained within twenty-four hours, surgical interference is the treatment of choice.

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107 East Eighty-Fifth Street

250 West Twenty-First Street

# TREATMENT OF GONORRHEAL VAGINITIS IN CHILDHOOD WITH ESTROGENIC SUBSTANCES

MARGARET A. LIMPER, M.D., AND ETHEL E. HIERONYMUS, M.D.
LOUISVILLE, KY.

FOLLOWING Allen's[1] experimental work on the effect of estrogenic substances on the vaginal epithelium of immature monkeys, Lewis[2] introduced the use of theelin in the treatment of gonorrheal vaginitis in children. Workers who had become discouraged with the results obtained with older types of treatment welcomed the innovation, and since the publication of Lewis' work in 1933 there have appeared in the literature seven reports,[3-9] dealing with 122 cases treated with various preparations of the estrogenic principle (Table I). In general, the results have been favorable, but there have been exceptions. The results reported with theelin have been uniformly favorable. Huberman and Israeloff[4] reported good results with an ethylene glycol solution of amniotin subcutaneously; Witherspoon,[9] using similar doses of the same substance, found desquamating epithelial cells but did not obtain a single cure. TeLinde and Brawner[8] did not observe the conversion of the immature to the adult type of vaginal epithelium with this substance and concluded that the one cure in this series was a coincidence; they obtained 77 per cent of cures with an oily solution of amniotin subcutaneously, and 100 per cent of cures with amniotin suppositories. With regard to oral treatment, Goldberg and his coworkers[7] concluded from a small series treated with amniotin that the results do not differ materially from those by hypodermic injection, although the dosage in units was larger. Nabarro and Signy,[5] using menformon, obtained fair results with oral administration. They advocate giving a large initial dose of the preparation intramuscularly and following this with oral administration; they used local treatment in conjunction with hormone therapy, but, on the whole, their results seem less favorable than those reported with the use of other preparations of the estrogenic principle. In contrast to these favorable reports of the oral method of treatment, TeLinde and Brawner concluded that amniotin administered orally is of no value.

The problems with which the various workers have been confronted are: (1) the possibility of harmful effects resulting from the administration of estrogenic substances to the child; (2) the optimum dosage for effective therapy; and (3) the duration of treatment after the smears have become negative.

From the Departments of Pediatrics and Gynecology, University of Louisville School of Medicine.

TABLE I

SUMMARY OF LITERATURE ON ESTROGENIC TREATMENT OF VAGINITIS

| AUTHOR | PREPARATION USED | ROUTE OF ADMINISTRATION | NO. OF CASES | RESULTS |
|---|---|---|---|---|
| Lewis | Aqueous theelin | Subcutaneous | 8 | 5 permanent cures<br>2 recurrences<br>1 reinfection (?) |
| Brown | Aqueous theelin | Subcutaneous | 7 | All cured |
| Huberman and Israeloff | Ethylene glycol Solution amniotin | Subcutaneous | 5 | All cured |
| | Amniotin oral | Oral | 1 | Cured |
| Nabarro and Signy | Menformon | Oral and intramuscular | 20 | 6 permanent cures<br>14 relapses, all successfully retreated |
| Reading | Aqueous theelin | Intramuscular | 2 | All cured |
| | Theelin in oil | Intramuscular | 6 | |
| Goldberg et al. | Amniotin oral | Oral | 6 | All cured |
| | Ethylene glycol Solution amniotin | Subcutaneous | 9 | 7 permanent cures<br>2 recurrences |
| | Combined | Oral and subcutaneous | 1 | Cured |
| TeLinde and Brawner | Amniotin oral | Oral | 6 | 1 cured |
| | Ethylene glycol Solution amniotin | Subcutaneous | 11 | 1 cured<br>1 recurrence |
| | Amniotin in oil | Subcutaneous | 18 | 5 recurrences<br>13 permanent cures |
| | Amniotin suppositories | Vaginal | 12 | 12 permanent cures |
| Witherspoon | Ethylene glycol Solution amniotin | Subcutaneous | 10 | None cured |

With regard to the first of these questions, Huberman and Israeloff[4] showed that amniotin has no cumulative action, as is evidenced by the constant presence of this product in the urine of the children receiving treatment, and that, while the renal threshold of the estrogenic substance varies in different individuals, the amount of the substance in the urine is directly proportional to the intensity of treatment. Hartman,[10] working with monkeys, showed that the threshold for vaginal bleeding was far below that at which estrous changes occur in the uterus and ovaries and believed that although the hormone might induce a temporary inhibition of growth changes in the ovarian follicles, this effect is transient, and produces no permanent damage to the ovaries. Allen and Diddle[11] have recently made measurements on the ovaries and uteri of monkeys before and after comparatively large doses of theelin and examined the follicles afterward. Although there was some inhibition of the growth of the larger follicles, they concluded that this was not sufficient to interfere with normal function. In his earlier work with monkeys, Allen[1] had found that involution of the structures affected occurred within a few weeks after the hormone was discontinued. In the clinical application of these substances, vaginal bleeding has not been noted in any of the cases. Abdominal pain occurred after the injections in a number of cases. Turgescence of the labia, some hypertrophy of the breasts, and the appearance of a few scattered pubic hairs were also noted in quite a number of instances. Lewis,[2] Goldberg and coworkers,[7] and TeLinde and Brawner[8] found that several weeks after the cessation of treatment, biopsies from the vaginal mucosa showed a regression to the infantile type. It is of some interest, however, that several of the workers observed that in the treatment of recurrences after hormone therapy some months previously, smaller doses were required for a cure than in the original treatment.

The accumulated evidence is against any permanent harmful effects from the administration of estrogenic substances to young girls; the final answer to the question, however, should probably await observations on the treated cases after puberty. It would seem desirable to limit the treatment to the smallest dosage and the shortest duration that will give consistently good results.

There is considerable variation in the dosage and duration of treatment recommended by various authors. Goldberg and his coworkers employed 100 to 400 rat units of amniotin orally, and an average of 50 to 150 rat units hypodermically for periods of 8 to 120 days. TeLinde and Brawner concluded that daily 100 rat unit doses of the oily preparation of amniotin subcutaneously were as effective as larger doses; in the children who were permanently cured with this preparation, treatment was continued on an average of twelve days after the smears had become permanently negative. Mazer[12] is using 1,000 rat unit doses of progynon-B every other day for a period of eight weeks.

Our material consists of twenty-seven cases, of which all except three were dismissed after hormone therapy (Table II); one of the latter is still under treatment for a recurrence. A number of other patients had some hormone therapy, but they came in irregularly or discontinued treatment without obtaining a cure. In the year that we have conducted our vaginitis clinic, we have also dismissed as cured five patients with other types of therapy, mostly local instillations of silver nitrate ointment, supplemented in a few instances with injections of gonococcus filtrate or antigen. These cures were effected in three, four, eight, nine, and ten months, respectively.

Our first patients were treated with small doses (50 to 100 rat units) of an ethylene glycol solution of amniotin subcutaneously three times a week. The doses were small partly because our funds were very much limited and also because we knew very little about the optimum dosage clinically. As will be seen from Table II, Patients 1 and 3 were apparently cured with only 500 and 400 rat units, respectively. Patient 3 has remained well for one year. Patient 6 continued to show positive smears with a similar dosage and was cured with larger amounts of amniotin in oil. Patient 2 had a recurrence, or possibly a reinfection, after an apparent cure with 1,050 rat units. We are listing Patient 8 as having a recurrence, but she probably was not cured with 500 rat units in spite of five negative smears, for her mother told us afterward that the discharge never cleared up entirely.

After treating a few patients with an oily preparation of amniotin, we began using progynon-B as a source of the estrogenic principle. Upon the suggestion of Dr. Charles Mazer, of Philadelphia, we increased our dosage considerably. He had been using 1,000 rat units every other day. We decided to experiment with half this dosage, and since the oily preparation is absorbed and excreted slowly, we felt that three- or four-day intervals between injections would probably be satisfactory. We have followed the reaction of the vaginal epithelium by instilling into the vagina one or two dropperfuls of saline, and examining the washings microscopically. After from four to six injections the discharge appears caseous rather than purulent. Microscopically, pus cells begin to disappear, while large clumps of epithelial cells appear, some of which can be seen to be definitely cornified. With a few exceptions, the smears were permanently negative after two to four weeks of treatment. We found that this effect could be obtained by twice weekly injections of the oily preparation of the estrogenic principle. Recently, we have reduced our dosage to 300 rat units, and our results are comparable to those obtained with 500 rat unit doses.

Our plan is to continue treatment of these patients for four weeks after their smears become permanently negative, or for a total of eight weeks. In those children whose smears become negative after ten days or two weeks, it is probably safe to reduce the period of treatment to

TABLE II

SUMMARY OF 27 CASES OF GONORRHEAL VAGINITIS IN CHILDHOOD TREATED WITH ESTROGENIC SUBSTANCES

| CASE | AGE IN YEARS | DURATION OF DISEASE | DOSAGE OF ESTROGENIC SUBSTANCE | TOTAL AMOUNT | DURATION OF TREATMENT IN DAYS | NO. CONSECUTIVE NEG. SMEARS BEFORE DISMISSAL | COMMENT |
|---|---|---|---|---|---|---|---|
| 1 | 3 | 2 wk. | 50 R.U. E.G.A.* x 10 | 500 R.U. | 25 | 5 | Checked after 6 wk. |
| 2 | 6 | 3 mo. | 50 R.U. E.G.A. x 12<br>100 R.U. E.G.A. x 5 | 1,100 R.U. | 37 | 5 | Followed by recurrence |
| | | | 250 R.U. O.A. x 8<br>125 R.U. O.A. x 8 | 3,000 R.U. | 51 | 7 | Negative after 7 mo. |
| 3 | 10 | 4 wk. | 100 R.U. E.G.A. x 5 | 400 R.U. | 60 | 7 | Negative for 1 yr. |
| 4 | 5 | 2 mo. | 125 R.U. O.A. x 6<br>250 R.U. O.A. x 3 | 1,500 R.U. | | | |
| | | | 500 R.U. P.B. x 7 | 3,500 R.U. | 115 | 8 | Checked after 1 mo. |
| 5 | 6 | 1 yr. | 125 R.U. O.A. x 12<br>250 R.U. O.A. x 2 | 2,000 R.U. | 42 | 8 | Followed 2 mo. |
| 6 | 7 | 6 wk. | 100 R.U. E.G.A. x 14<br>50 R.U. E.G.A. x 8 | 1,800 R.U. | | | |
| | | | 125 R.U. O.A. x 4<br>250 R.U. O.A. x 7 | 2,250 R.U. | 105 | 9 | Checked after 3 mo. |
| 7 | 1¼ | 2 wk. | 125 R.U. O.A. x 5<br>100 R.U. once<br>250 R.U. O.A. x 2 | 1,225 R.U. | | | |
| | | | 500 R.U. P.B. x 11 | 5,500 R.U. | 56 | 8 | Checked after 3 mo. |
| 8 | 7 | 6 mo. | 100 R.U. O.A. x 5 | 500 R.U. | 10 | 5 | Followed by recurrence |
| | | | 500 R.U. P.B. x 10 | 5,000 R.U. | 32 | 7 | Negative after 1 mo. |
| 9 | 6 | 18 days | 500 R.U. P.B. x 19 | 9,500 R.U. | 63 | 7 | Checked after 1 mo. |

*Key to table: E.G.A., ethylene glycol solution—amniotin
O.A., amniotin in oil
P.B., progynon-B in oil
F.M., folliculin menformon.

TABLE II—CONT'D

| CASE | AGE IN YEARS | DURATION OF DISEASE | DOSAGE OF ESTROGENIC SUBSTANCE | TOTAL AMOUNT | DURATION OF TREATMENT IN DAYS | NO. CONSECUTIVE NEG. SMEARS BEFORE DISMISSAL | COMMENT |
|---|---|---|---|---|---|---|---|
| 10 | 6 | ? | 1,000 I.U. F.M. x 4<br>1,500 I.U. F.M. x 2<br>2,000 I.U. F.M. x 9 | 25,000 I.U. | | | |
| | | | 250 R.U. O.A. x 6<br>125 R.U. O.A. once | 1,875 R.U. | 57 | 5 | Smears negative after 47 days |
| 11 | 8 | ? | 125 R.U. O.A. x 10<br>250 R.U. O.A. x 3 | 2,500 R.U. | | | |
| | | | 500 R.U. P.B. x 21 | 10,500 R.U. | 80 | 9 | Not checked |
| 12 | 7 | 6 mo. | 500 R.U. P.B. x 10 | 5,000 R.U. | 53 | 7 | Followed by recurrence |
| | | | 300 R.U. P.B. x 8 | 2,400 R.U. | 52 | 8 | Checked after 2 mo. |
| 13 | 2½ | Chronic | 500 R.U. P.B. x 9 | 4,500 R.U. | 29 | 11 | Not checked |
| 14 | 4 | 2½ mo. | 500 R.U. P.B. x 13 | 6,500 R.U. | 33 | 10 | Followed 3 mo. |
| 15 | 6 | ? | 1,000 I.U. F.M. x 31<br>2,000 I.U. F.M. x 25 | 81,000 I.U. | 60 | None | Left hospital with positive smear |
| 16 | 7 | 1 mo. | 500 R.U. P.B. x 8<br>250 R.U. P.B. once | 4,250 R.U. | 29 | 7 | Followed 5 mo. |
| 17 | 2 | ? | 500 R.U. P.B. x 9<br>300 R.U. P.B. x 2 | 5,100 R.U. | 36 | 8 | Followed 2 mo. |
| 18 | 9 | 4 yr. | 500 R.U. P.B. x 7<br>300 R.U. P.B. x 8 | 5,900 R.U. | 50 | 11 | Smears negative after 2 wk. treatment<br>Checked after 6 wk. |
| 19 | 4 | 7 days | 500 R.U. P.B. x 6<br>250 R.U. P.B. x 1<br>300 R.U. P.B. x 10 | 6,250 R.U. | 60 | 7 | Smears negative after 4 wk. treatment<br>Checked after 1 mo. |

TABLE II—CONT'D

| CASE | AGE IN YEARS | DURATION OF DISEASE | DOSAGE OF ESTROGENIC SUBSTANCE | TOTAL AMOUNT | DURATION OF TREATMENT IN DAYS | NO. CONSECUTIVE NEG. SMEARS BEFORE DISMISSAL | COMMENT |
|---|---|---|---|---|---|---|---|
| 20† | 6 | 3 days | 500 R.U. P.B. x 6<br>250 R.U. P.B. x 1<br>300 R.U. P.B. x 11 | 9,050 R.U. | 88 | 6 | Followed by recurrence after 2 days |
| | | | 300 R.U. P.B. x 8 | 2,400 R.U. | 35 | 9 | Negative after 2 wk. follow-up |
| 21 | 7 | 7 days | 500 R.U. P.B. x 9<br>300 R.U. P.B. x 7 | 6,700 R.U. | 57 | 11 | Smears negative after 2 wk. treatment |
| 22 | 9 | 10 mo. | 500 R.U. P.B. once<br>300 R.U. P.B. x 12 | 4,100 R.U. | 80 | 9 | Smears negative after 4 wk. |
| 23 | 8 | 8 mo. | 500 R.U. P.B. x 6<br>300 R.U. P.B. x 7 | 5,100 R.U. | 57 | 10 | Smears negative after 2 wk. treatment |
| 24 | 6 | 17 mo. | 300 R.U. P.B. x 14 | 4,200 R.U. | 54 | 10 | Negative after 4 days' treatment |
| 25 | 3 | 8 days | 300 R.U. P.B. x 13<br>400 R.U. P.B. once | 4,300 R.U. | 67 | 8 | Negative after 4 wk. treatment Checked after 6 wk. |
| 26 | 2 | 13 days | 300 R.U. P.B. x 15<br>400 R.U. P.B. once | 4,900 R.U. | 63 | 6 | Smear negative after 36 days' treatment |
| 27 | 5 | 2 mo. | 500 R.U. P.B. x 5<br>300 R.U. P.B. x 8 | 4,900 R.U. | 56 | Pos. | Not dismissed |

†Discharged as cured since completion of this article.

six weeks. The minimum number of negative smears for dismissal is five, and we attempt to check again six weeks after treatment has been completed. Many of our earlier patients had had unsuccessful local therapy before estrogenic treatment was begun. The only local treatment used in conjunction with hormone therapy has been external cleansing for the patient's comfort, and, in a few cases in which irritation was marked, sitz baths have been recommended for a period of a week or ten days.

As will be seen from Table II, 24 of the 27 cases may be regarded as having obtained cures from hormone therapy. One of the failures (Case 15) was in a patient treated with folliculin menformon. Our experience with this preparation was limited, but we believe it is less effective than the other two substances used. Patient 27 discontinued treatment of her own accord after thirteen injections over a period of eight weeks, with a positive smear on her last visit to the clinic. The recurrences in Cases 2 and 8 have been referred to above. Under our present routine of therapy, we have had two recurrences. Patient 20 required eight weeks of treatment before the smears became negative. She was treated for two weeks after the smears became permanently negative but developed a recurrence after thirty-eight days. She is at present under treatment for the recurrence. Patient 12 came in so irregularly for treatment that it is uncertain whether she had a recurrence or simply a "false cure." We have not calculated the average dosage or the average duration of treatment because most of the longer periods of treatment have been in patients who came in irregularly for injections. Our social service work has been inadequate, and we have been unable to follow these cases as closely as we would like.

Our giving the oily preparations of the hormone intramuscularly probably accounts for the fact that we do not observe the pain TeLinde and Brawner describe as associated with the subcutaneous injection of amniotin in oil. A 20 gauge needle is used, and the injections are given into the gluteal muscles on alternate sides. After the needle has been introduced, there is no complaint of pain, and there is no soreness during the period of absorption. We buy the progynon-B in concentrated form, and dilute it with oil of sesame so that 0.1 c.c. contains 100 rat units of the hormone; the total volume of each injection is therefore small.

Because of limited funds, we have been unable to use suppositories in treating any of our patients. TeLinde and Brawner obtained 100 per cent cures by this method and only 77 per cent cures in the patients treated with amniotin in oil. Because they found that less of the hormone was required for a cure when the suppository method was used; and since there were no breast changes with this method, they concluded that there is some local action which takes place as a result

of an increased concentration of the drug in the pelvic tissues. The method is certainly worthy of further trial and study.

Hypertrophy of the genitals or of the breasts was not observed in any of our patients. One patient developed a minute cyst of the nipple, and a few patients developed a few scattered pubic hairs. Several of the patients treated with subcutaneous amniotin developed skin eruptions which may have been due to the injections.

## SUMMARY

1. In four cases of gonorrheal vaginitis treated with an ethylene glycol solution of amniotin, there were two permanent cures and two recurrences.

2. With oily solutions of amniotin or of progynon-B administered intramuscularly twice weekly, conversion from the infantile to the adult type of vaginal mucosa was observed, and cures were obtained in all except two cases.

3. One patient treated with folliculin menformon daily for sixty days failed to respond to treatment.

4. No harmful effects as a result of injections were observed.

We wish to thank Dr. J. A. Kennedy and the Bacteriology Department for their cooperation, Dr. Hugh R. Leavell, City Health Director, for his financial support, and the members of the Social Service Department for their assistance.

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# American Academy of Pediatrics

## Proceedings

### SIXTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

KANSAS CITY, MISSOURI, MAY 11 AND 12, 1936

**Round Table Discussion on Appendicitis**

Chairman: Dr. Albert H. Montgomery, Chicago.

Assistant: Dr. Joseph Brennemann, Chicago.

CHAIRMAN MONTGOMERY.—It probably seems incongruous to you to have a surgeon head a round table discussion of this kind. However, when my colleague, Dr. Joseph Brennemann, kindly consented to participate in the discussion I thought that perhaps our experience extending over fifteen years in which we have seen together about 1,000 cases of appendicitis in children might give us some ideas that would be interesting for a discussion of this topic. I trust that our impressions and yours may be helpful in promoting a clearer understanding of this rather common disease in children and in reducing the unjustifiable mortality which prevails at present.

It is a strange commentary on modern medicine that a disease like appendicitis with which we have been rather familiar for fifty years and of which our knowledge of the etiology, pathology, symptoms, diagnosis, and treatment is rather complete, should show a rise instead of a decline in the mortality statistics. It is very timely, therefore, for those of us who are called upon to treat abdominal conditions in children to take stock of our present knowledge and see if we cannot in some way prevent a fatal termination in the patients that are afflicted with this disease.

In order to promote a logical discussion of this subject it would seem appropriate to me to call upon a man who can give you the impressions of the pediatrician who sees these patients first and on whom rests the burden of making a correct diagnosis and advising prompt and proper treatment.

#### Appendicitis in Children

Joseph Brennemann, M.D., Chicago

In the last fifteen years we have had nearly 1,000 cases of appendicitis at the Children's Memorial Hospital. The medical and surgical departments cooperate very closely and sympathetically and Dr. Montgomery and I have seen most of these cases and have mulled over an equal, or larger, number of abdominal conditions that called for confirmation or exclusion of a possible diagnosis of appendicitis. It seemed to both of us that the main discussion should begin with a presentation of the subject as it attacks the first line of defense, the pediatrician and the general

practitioner. We all know that the one important point in treatment and resulting prognosis is an early diagnosis. The surgeon sees relatively few cases first hand. He is usually called in to confirm the diagnosis and to treat the patient after he has been seen by someone else. The pediatrician and the general practitioner see many more patients with abdominal pain not due to appendicitis than due to that condition. They must, therefore, not only be able to recognize the disease when present, but even much more often, to exclude it. The diagnosis is by no means always easy, or carefree, even by those with a large experience in a charity hospital where such cases are enormously more frequent than in a busy pediatric or general practice. This is also evident in the frequency with which appendicitis is diagnosed when it is not present, and also not diagnosed as such when it is present. The difficulty that is inevitable in the medical diagnosis of abdominal conditions of which pain and tenderness are a part is, however, a minor contribution to the unfortunate fact that the mortality and serious morbidity of appendicitis are still higher than the conditions would warrant under favorable circumstances. In spite of the fact that we are usefully informed as to the etiology and quite fully informed as to the morbid anatomy, symptomatology and ideal treatment, the mortality and serious morbidity are not decreasing, and probably will not for some time to come. The major factor in this deplorable condition seems evident. The appendix is an insignificant little organ, if one may call it so, that is important only because of its location. When inflamed it causes relatively little pain early, the all-important tenderness is not sought for, and there is little fever. The laity are apt to estimate the seriousness of a disease by the degree of pain and the height of the temperature. They will call a physician for a colic, or for a banal throat infection with a fairly high fever, and will interpret a case of appendicitis as a mere "stomach ache" or "intestinal upset." The almost inevitable vomiting clinches the interpretation and from time immemorial one or more cathartics are supposed to be prescribed when there is any abdominal, stomach, or bowel trouble. This situation is almost the rule in our experience. A doctor is finally called in at the end of twenty-four or forty-eight hours, or longer, the appendix has now ruptured and the mortality and serious morbidity have gone from near zero to 5 or 10 per cent. The prognosis of appendicitis is, therefore, more dependent on the intelligence and alertness of the parents than on any other one factor. For that reason statistics of results in private and charity practice are not comparable—are even misleading. It is evident, too, that a major factor in prophylaxis is lay education, a difficult problem.

The etiology of appendicitis is probably not to be found in a single factor and there is, as a result, some difference of opinion. The surgeon who usually sees only the local condition is naturally impressed by the presence of a fecalith, kinking, narrowing, bands, adhesions, even pinworms, and so leans toward an enterogenous or mechanical causation. The pediatrician, who examines the throat in every patient and is cognizant of the fact that the lymphoid tissue of the appendix so closely resembles that of the tonsils that the former has been spoken of as the abdominal tonsil and appendicitis as abdominal angina, so frequently finds a throat infection as a forerunner of appendicitis that he feels very confident that such infections have a very definite etiologic relationship to appendiceal inflammation. One can hardly expect the surgeon to be interested in, or properly interpret, a throat. Appendicitis has been seen many times to follow measles, scarlet fever, and other infections, and may possibly be more frequent with infections of the throat only because they are so much more frequent than all others combined. It is interesting in this connection to recall that Evans, among students in the University of Wisconsin, reported eight times as many cases of appendicitis during periods of grippy epidemics as in nonepidemic times.

The cardinal symptoms of appendicitis are pain and tenderness in the abdomen, vomiting, and a low temperature. As I said before, the appendix is a relatively little organ and one cannot expect either much pain or fever when it is inflamed and uncomplicated. If there is very severe pain, it speaks against appendicitis; not always, as we learned from a recent patient who apparently had excruciating pain. It was one of those exceptions that emphasizes the rule. A high fever speaks against an early, uncomplicated appendicitis, and the cause can usually be found elsewhere, usually in the throat or in the lungs. I recall a patient that I saw in consultation, with a temperature of 105.6° F., and just coming out of a third convulsion. He had a throat infection and an otitis media—but also a point of tenderness in the lower right quadrant of the abdomen. I emphasized the fact that the appendix should be watched. The next morning the temperature had sunk to the usual appendiceal level, there was still local tenderness, but the condition was interpreted as improved, not by myself, because the fever was lower. Two days later the child was brought to the hospital with a ruptured appendix, by another physician.

As in the adult, the pain usually starts in the epigastrium or about the umbilicus, and soon migrates to the region that is involved. In this it differs with the far more important sign of tenderness, the one significant and unfailing sign, which is always at the point of involvement. If there is early diffuse tenderness, it speaks against appendicitis—again, not always. Inasmuch as the appendix may occupy various positions, especially the part that is acutely inflamed, this tenderness, while usually at or near McBurney's point, may be high or in the flank in retrocecal appendicitis, low down near Poupart's ligament, or even on the left side. We had a child with the pain and tenderness on the left side because of a complete situs inversus; several in which the inflamed tip of the appendix lay across the midline and the point of tenderness was to the left of the left border of the left rectus muscle. Because of tenderness, it is sometimes of diagnostic value to bear in mind that colicky pain from any cause invites pressure, while inflammation brings out defense against pressure.

Rebound tenderness is stressed by some examiners. It has never seemed to me of determining significance in diagnosis. *I think it cannot be emphasized too heavily that the one important sign of early appendicitis is tenderness at one point, in the proper clinical setting.* It is not pathognomonic, however.

Rigidity is an important sign if present, but must not be looked upon as a desideratum. Early there may be none. A little later there is always a voluntary defense against the pain of pressure. When the rigidity becomes involuntary, instant and boardlike to any degree of pressure, peritonitis has supervened.

Except under certain conditions I do not feel that rectal examination is indicated in children. It is an extremely unpleasant procedure, a bad thing in itself unless necessary, and this often overshadows any information that may be obtained if that is not more easily and usefully elicited by external examination. It is of distinct value in determining purely objective conditions, such as a mass in late appendicitis or as a postoperative complication, especially if there is a question as to whether an abscess is pointing in that direction.

Vomiting is almost unfailing—but not quite. It has some diagnostic value—negative rather than positive. I have the impression that surgeons value it too highly because they are not as familiar with the fact, as we are, that young children vomit with nearly every infection.

The leucocyte count has a predilection for somewhere between 15,000 and 20,000—but must never alone be considered of determining diagnostic value. We have seen it all the way from 5,000 to 30,000, or more. A very low count has often a bad prognosis—a very high count may, or may not have. An increase or a de-

crease in the white blood count is, on the other hand, of a great deal of significance as to progress in a doubtful or possibly receding case.

There is a point in the examination that I think bears emphasis. It is, of course, axiomatic that the examining hand must be warm, laid on flat, that the pressure must be gentle and must proceed from the unaffected to the affected side. I have an impression that the experienced surgeon is more gentle in his examination than is the pediatrician, or general practitioner, not to mention the interne, because he is more concretely familiar with the morbid anatomy and the potential danger of kneading an appendix that is about to rupture. The point that I want to stress is that it is not only useless, as a rule, but may also be misleading to keep asking with each poke whether this place hurts, or that one, etc. Far more reliable and certain information can be obtained by merely watching the child's face, or noting some expression of defense such as a squirm or a motion of the hand toward the tender spot. A wince is more decisive than a "yes" or a "no" and even a child that is appendicitis-conscious may dissemble by words, rarely by actions.

So far I have discussed only the earlier stages of appendicitis. In a way they run a fairly constant course and the diagnosis is usually easy. As a rule they run a day or even two without alarming symptoms. Only rarely does one see a fulminating case. And yet one came to us recently with a ruptured, gangrenous appendix in a child who was actively playing and apparently symptom-free six hours before.

Following the early course one of three things happens:

1. The symptoms and signs disappear and the inflammation recedes. This is not uncommon. If there is an undoubted recession it is probably best not to operate at the time, but to advise a later operation because of the probability of a recurrence.

2. The appendix ruptures and there is a spreading peritonitis. This calls for operation at any time.

3. The appendix does, or does not, rupture and a well-defined, sharply circumscribed mass ensues. These patients, as usually seen on the third or fourth day of the disease, do not appear alarmingly sick—often have a sort of convalescent look about them. We have seen a good many such cases and both Dr. Montgomery and I feel very strongly that they should not be operated upon at the time, and we have never regretted it. They must, of course, be watched closely and in a hospital. We have seen masses as big as my fist recede completely and rather quickly. They should always be operated later, not less than a month, preferably longer, after the complete disappearance of the mass.

Dr. Montgomery will discuss the treatment in detail, but I couldn't resist saying as much as I did from the pediatric standpoint.

We come, finally, from our standpoint, to the all important matter of diagnosis. Once made, the treatment usually follows naturally. In both of these points I cannot share the optimism and complacency of a pediatric friend who said, anent this discussion: "What is there to it? You make the diagnosis and then have them operated." We somehow still have plenty of trouble and once in a while we make a mistake—one way or the other. We never hide behind an "injected appendix"—we expect a certain small number of errors in diagnosis.

Probably the largest source of diagnostic unhappiness is the child who has a pain in the abdomen that one does not feel justified in ascribing to appendicitis. They are much more common in practice than is appendicitis. I am skeptical about indigestion and gas pains and if there is such an entity as spastic colon in childhood, it has been above the threshold of my diagnostic acumen. I have a suspicion that the allergists have allocated most of these pains to their special field. Maybe they belong there. To me they are still a mystery.

Pneumonia occasionally, but rarely should, leads to an error in diagnosis. The pain of the accompanying pleurisy is usually below the diaphragm—much more rarely in the corresponding shoulder. The general appearance, the high fever, the flaring alae nasae, the expiratory grunt, the rapid respiration, the flushed face and the high leucocytic count rarely leave any doubt. Bearing in mind that suppression of breath sounds is the earliest sign of lobar pneumonia may help. It unfortunately occurs, too, in appendicitis, though in less degree. A roentgenogram is usually decisive and should never be omitted if in doubt and if obtainable. It must be remembered, however, that both conditions may be present. Much that has been said applies also to pleurisy itself and even to acute pericarditis.

The late Carnet, of Philadelphia, wrote extensively on the frequency with which intercostal neuralgia was confused with appendicitis. In the former the tenderness was said to be superficial—in the latter, deep. If, after tensing the abdominal muscles, the tenderness persisted he attributed it to intercostal neuralgia; if not, to appendicits. I was always skeptical about his observations until I unexpectedly visited him at his hospital. He showed me several that seemed convincing.

Gallstones and renal colic hardly enter into the picture.

Pyuria is more often weighed in the balance by the surgeon than by the pediatrician. Probably the commonest cause of a transient pyuria is an upper respiratory tract infection and appendicitis may be present from the same source. Pyuria should not exclude appendicitis. The surgeons tell us that pyuria may result from contact of a ureter with an acutely inflamed appendix. I have never been able to diagnose that condition.

So-called primary peritonitis is often impossible to differentiate from a late appendicitis with spreading peritonitis. The differentiation is important because operation is indicated in the latter and probably contraindicated in the former. If there is a history of pain and tenderness in the right lower quadrant at the beginning of the disease, or if it still predominates in that region, one naturally leans toward the diagnosis of a spreading peritonitis following appendicitis. As a rule the differentiation is not difficult. In primary peritonitis the child is usually very sick from the start and there is pain and exquisite tenderness over the whole abdomen from the very beginning. I am inclined to think that we have been overcautious in not resorting more often to diagnostic puncture as proposed by Denzer fifteen years ago and again emphasized in the June, 1936, number of the JOURNAL OF PEDIATRICS.

A right-sided twisted ovarian pedicle with strangulation may closely simulate appendicitis. Dr. Montgomery once made the diagnosis from the nature of a mass felt per rectum. I have advised him not to try it again! A very high leucocyte count is characteristic and of considerable diagnostic value. One of our patients had a count of 80,000, and led the interne, who had recently had a gynecological service, to suggest the diagnosis from that observation. Fortunately, operation is indicated in both cases.

A perforating or inflamed Meckel's diverticulum can hardly be differentiated from appendicitis unless there is a coincidental hemorrhage from the intestines. A diverticulitis, in the usual sense, I have never encountered.

One of the most frequent and puzzling conditions that call for differentiation is the abdominal pain that occurs with such diseases as measles, scarlet fever, pneumonia, and, more frequently than with any other, upper respiratory tract infections. A child entered the ward acutely sick with a strong suspicion of appendicitis. We delayed because she was too sick and had too high a fever for appendicitis. The next morning she presented the picture of a florid scarlet fever. On this point it is rather unavoidable not to inject a personal matter. Some years ago (1921)

I wrote a paper on "The Abdominal Pain of Throat Infections," in which I reported the frequent occurrence of pain in the abdomen, in fact two types of pain, with upper respiratory tract infections. One of these usually occurs early, is transient, has a colicky, neuritic quality, is practically always restricted to the region of the umbilicus and suggests a referred origin. The other usually occurs a little later, is more dull, diffuse and persistent, is not restricted to any one locality but is probably found more often in the lower right quadrant and is accompanied by tenderness somewhat less marked than that of appendicitis. There is every reason to believe that the latter type is due to mesenteric lymphadenitis. Such glands are not infrequently found at operation for appendicitis, erroneously diagnosed, as well as at necropsies of patients dying of grippy infections. I have known of several instances in which they have ruptured, making a differentiation from appendicitis impossible except at operation. Following the publication of that paper apparently a number of people had read at least the title, not the conclusions, because I saw several cases of appendicitis in consultation in which the diagnosis was missed because the child had an evident throat infection. I then went back over the last ten cases of appendicitis I had seen in practice and found that nine of them had such evidences of an immediately preceding, or present, throat infection, as tonsillitis, mastoiditis, otitis media, grippe, pneumonia, cough, etc. One child seen in consultation had a severe throat infection and a tender distended abdomen. It was my impression that the child had a throat infection, a right lower lobe pneumonia, a ruptured appendix and a general peritonitis. My impression was questioned, a blood transfusion (!) was given and further treatment was put off to await the result of an x-ray examination on the following morning. The necropsy that afternoon confirmed the fact that all of the things that had been suspected can follow, or accompany, an initial infection in the throat. So I wrote another paper with the purposely clumsy title of "The Abdominal Pain of Throat Infections, and Appendicitis" (1927) pointing out the unquestionably frequent association of the two conditions. This idea is not new, and I have already quoted Evans' experience at the University of Wisconsin. I am convinced that more than 50 per cent of the cases of appendicitis are secondary to infections in the throat. Because of the above experience I am anxious to leave this final impression: If clinical evidence in a child points to appendicitis and the child has at present, or had an immediately preceding, throat infection, lean toward rather than away from the diagnosis of appendicitis—or better still wholly disregard the throat.

CHAIRMAN MONTGOMERY.—Speaking from the standpoint of the surgeon, I wish to ask your attention to the anatomy of the appendix for I feel that it has a definite bearing on the clinical aspects of appendicitis as we see it in children. In infants the appendix is a cone-shaped affair with an open, wide mouth that permits free emptying into the cecum. This explains very clearly why obstruction does not occur in the organ and as a consequence, appendicitis is very rare at this age. When we recognize that most appendicitis occurs at the tip or distal portion of the organ or at the side of a fecolith, scar, constricting band, or twist, it seems very definite that primarily appendicitis is caused by something that obstructs the emptying of this blind tube. In children past the age of infancy such findings at operation are very common. Even when we do not find a definite obstruction there is often a kink of the appendix caused by a short mesentery which may not produce a definite appendicitis but may cause attacks of appendiceal colic.

Another anatomical point in connection with the clinical picture is the indefinite location of the appendix. In most instances, of course, it will be located in the right lower quadrant of the abdomen, hanging over the brim of the pelvis or point-

ing upward toward the spleen. When it is in the pelvis, the tip may rest on the left side of the mesentery and if an abscess forms it may produce a mass on the left side of the abdomen. In other cases the appendix is without a mesentery and rests behind the peritoneum in the retrocecal portion. In such cases the point of maximum tenderness will be on the right side posteriorly toward the loin. An inflamed appendix in that location is apt to produce a spreading cellulitis if it ruptures and prove fatal by extending retroperitoneally. Again, anatomically, the colon may not rotate completely and the appendix may be situated high up in the right side near the gallbladder. High abdominal pain and tenderness and occasionally a mild jaundice may produce a very confusing clinical picture in such cases. In rare instances the appendix may be located in the left lower quadrant of the abdomen with or without a situs transversus of the other organs. In that position it may simulate very much the picture of diverticulitis which is practically unknown in children but common in adults.

Coming now to the symptoms, it should be emphasized that the entire clinical picture is usually composed of symptoms of a mild degree which are entirely out of proportion to the seriousness of the condition. The pain is usually colicky but rarely of a severe type. Vomiting is generally present, but not often repeated and may be entirely absent. Nausea, however, is practically always constant. Localized tenderness is probably the most reliable sign and should always be carefully looked for. It is most marked over the site of the inflamed appendix and is the best guide for the surgeon in his search for the pathology. Rigidity in my experience has not been present nearly as often in children as in adults, but a slight degree of muscular fixation over the point of tenderness is a very important and suggestive sign which may be revealed by careful palpation.

I do not believe the blood examination has the relative value that most diagnosticians give to it. A polynuclear leucocytosis of 15,000 or 20,000 is usually present but a leucocytosis above that figure should suggest the probability of a pneumonia or some other trouble. On the other hand, a leucopenia is of considerable importance in ruling out such conditions as typhoid fever, measles and influenza. In any event, the absence or presence of a leucocytosis should not be the deciding factor when all other signs and symptoms point to appendicitis.

When we come to the differential diagnosis, there is a large number of conditions that must be taken into consideration. Some of these are very easily ruled out but certain ones may be rather difficult. The main thing for the diagnostician is to keep in mind all of the pathological conditions that cause abdominal pain and be sure that they are ruled out as definitely as possible before making a final diagnosis. It is well known that in children chest conditions such as pericarditis, pleurisy and pneumonia frequently cause pain which is referred to the abdomen, often accompanied by abdominal tenderness and rigidity. A careful physical examination and an x-ray film of the chest will usually be sufficient to settle the diagnosis. Lymphadenitis of the mesentery glands has frequently been a cause of diagnostic error in our cases. Where bovine tuberculosis is present in a community an x-ray film of the abdomen may show calcified glands. Otherwise the clinical picture is so similar to that of appendicitis that I know of no way in which a definite diagnosis can be made. In such instances we have always felt that it was better to err on the side of safety and open the abdomen as none of these children have had any bad effects from the exploratory laparotomy.

Another rather confusing condition is the inflammation that often occurs in patients who have a Meckel's diverticulum. Some observers say that the tenderness in this condition is most marked a little below and just to the right or left of the umbilicus, but the clinical picture in general is so much like that of appendicitis that a differential diagnosis is usually impossible. However, as the treatment of

both conditions is essentially the same, the question of a definite diagnosis is only of academic interest. If at operation the appendix appears to be normal the surgeon should not forget to look carefully for a Meckel's diverticulum. By doing so he may solve his diagnostic problem and save his patient.

Tuberculosis of the spine may cause abdominal pain from the pressure on the nerves. A simple examination of the back for Pott's disease will usually clear up this question. Although pyelitis in girls frequently causes abdominal pain, the temperature and the leucocyte count are usually much higher and the patients are more toxic than is usually noted in appendicitis. Pus, of course, is present in the urine, but this may occur also in appendicitis if the tip of the inflamed appendix rests against the right ureter, and if there is any doubt about the matter an operative exposure of the appendix is the only safe course to follow. As a rule, conditions of the pelvic organs in girls do not often come into question. Tuberculous infections are very rare, but occasionally the pedicle of an ovarian cyst may become twisted and give a clinical picture that is rather suggestive of appendicitis. In one such case we were able to make a correct differentiation by means of a bimanual examination of the pelvis in the presence of a high leucocyte count. The onset of menstruation in girls at the age of puberty may be accompanied by sharp abdominal pain, but the general signs of appendicitis will be absent.

In peritonitis due to the streptococcus or pneumococcus which we see not infrequently in children the patients are usually more toxic than they are with appendicitis and the abdominal tenderness and rigidity are usually rather marked over the lower half of the abdomen. A differential diagnosis is often impossible to make and because of this we have felt that it was better to open the abdomen rather than to overlook a possible appendicitis.

Lymphadenitis affecting the iliac glands occurs not infrequently with tenderness low down in the abdomen. These patients often exhibit a tendency to fixation of the hip and a swelling may be present just above Poupart's ligament due to pus forming under the iliac fascia. There is a number of other conditions, of course, that occasionally have to be considered in the differential diagnosis, but I have tried to bring out the important and common ones that have given rise to confusion in our cases.

The treatment of appendicitis has been a matter of discussion for many years. I think we all agree that cases seen in the first twenty-four to forty-eight hours should be treated by operation at the earliest possible moment. There is a difference of opinion, however, as to what should be done when the disease has been present for a longer period of time. In our clinical experience we have encountered a number of patients who are not seen until this latter stage, and in this group we feel that if we can palpate a mass in the abdomen it is better to use conservative measures such as rest, subcutaneous fluids, hot applications, and no food by mouth. Nature is evidently trying to localize the process in these cases and an operation may cause a spreading of the infection and do more harm than good. During our conservative regime we watch these masses carefully. Many of them disappear completely after a few days and the patient's general condition gradually approaches normal. We advise such patients to return to the clinic after six or eight weeks for an appendectomy. If the abdominal mass instead of receding gradually increases in size, an abscess is evidently present and surgical drainage is advisable when the exact site of the pus is evident. However, in these later cases if the signs of appendicitis are present and no abdominal mass is palpable, we feel that localization has not taken place and that operative treatment is advisable at the earliest possible moment.

The complications that may arise in association with appendicitis are numerous and they frequently involve the diagnosis if they begin to appear within twenty-

four to forty-eight hours after the onset of the attack. A careful palpation may reveal a mass in the right lower quadrant which is evidently an effort on the part of nature to localize the infection to the region of the appendix. Pathologically, it is made up of the omentum and the adjacent coils of small bowel which become adherent to the appendix and very often to the parietal peritoneum. In the course of time this inflammatory mass may go on to abscess formation or it may entirely disappear. Watchful expectancy in such cases is usually wise and advisable. An ileus or intestinal obstruction is very apt to occur in an appendix that is situated between the ileum and the ascending colon. The possibility of this complication should be thought of when the appendix is found in this location at the time of operation. A prophylactic enterostomy made by placing a tube in the ileum will prevent any serious effects of this complication.

Peritonitis is, of course, the most frequent and serious complication of this disease. In many cases it begins gradually as a spreading process which can usually be recognized by the increased area of tenderness and rigidity in the lower abdomen together with a rise in the temperature and a more toxic generalized condition. An immediate operation to remove the source of the spreading infection is indicated. When the peritonitis has become generalized, rupture of the appendix has usually taken place and the clinical picture is very evident. In such cases a rapid simple operation to remove the appendix and institute drainage should be done. However, in the most severe cases where the patient is moribund, an immediate operation would possibly be fatal and a conservative treatment should be employed for about twenty-four hours. By this means some of these very bad cases can be improved sufficiently in twelve or twenty-four hours so as to withstand the strain of an operation.

Subphrenic abscesses in children usually come from infection which spreads up along the right colon gutter from the appendix. It is a late complication and unless it is thought of and carefully looked for, it may not be recognized. Whenever a patient continues to have a fever for some days after the appendiceal operation, the possibility of a collection of pus between the diaphragm and the liver should come into question. Immobility and elevation of the diaphragm in a fluoroscopic examination is very suggestive. The careful use of the exploratory needle followed by an immediate operation to promote drainage is indicated.

In a number of cases where an elevation of temperature and other signs of sepsis persist after operation, a pelvic abscess is the most likely complication. Abdominal and rectal palpation will usually show the presence of an inflammatory mass. Many of these abscesses will rupture into the rectum and evacuate spontaneously and they should be given an opportunity to do so. Otherwise surgical drainage should be established at the point where the pus seems to be most superficial. Fecal fistulas occur rather frequently in cases where a tube has been placed in the wound for drainage, but these fistulas usually close as the wound granulates and do not require any surgical treatment.

## GENERAL DISCUSSION

DR. BRENNEMAN.—I want to emphasize that there is often a bad delay because some doctors put too much importance in the blood count. Cases of mesenteric gland involvement are very interesting. A good many of them are associated with upper respiratory infections. Dr. Montgomery mentioned subdiaphragmatic abscesses from a ruptured appendix. I do not recall seeing any of these until the last four or five years, but during this period we have had an epidemic of them.

CHAIRMAN MONTGOMERY.—They are not frequent but should be considered.

DR. BRENNEMANN.—This abscess often contains air. I have seen Dr. Montgomery take an aspirating needle and poke around through the back until he finally locates the pus. This looks dangerous to me but I know of no harm ever resulting from this procedure.

Another problem is seen in young girls with abdominal pain who are about to menstruate.

DR. B. FEINBERG (PROVIDENCE, R. I.).—No mention of intussusception has been made as a complication of appendicitis or as a difficulty in differential diagnosis. One out of four acute abdomens I have seen has been due to obstruction. One case was a boy eight years old who developed an intussusception due to to a polyposis. Another case had had an upper respiratory infection for two or three days, then a localized pain in the usual area and presented a picture of a beginning acidosis. The white count was 5,000. At operation a normal appendix was found and an intussusception. In my experience very few cases of intussusception have had bloody stools, but have been diagnosed because of the characteristic pain.

CHAIRMAN MONTGOMERY.—Dr. Feinberg has had a very unique experience with his cases of intussusception because that number of cases at those upper ages is most unusual. Ninety per cent of intussusceptions occur under two years of age. This usually does not present much of a problem. In my experience in cases over three or four years of age, I see hundreds of cases of appendicitis to every intussusception. There are usually other conditions present such as polyposis in cases of intuzsusception in older children.

DR. FEINBERG.—In my locality, we divide our cases into two groups. They are acute abdomens or not acute, that is, there are those which should be opened immediately and those which should be considered conservatively. There is the problem of streptococcal and pneumococcal peritonitis.

CHAIRMAN MONTGOMERY.—The difficulty with pneumococcal and streptococcal cases is to know what is going on. The average results are just about as good with conservative management as with radical. There is the possible value of using a needle to aspirate some abdominal fluid to determine the organism present. The diagnosis of a ruptured graafian follicle which has been confused with appendicitis is usually made by the surgeon.

DR. BRENNEMANN.—Henoch's purpura might be confusing but usually in this condition the purpura develops early, thus making clear the diagnosis.

DR. SIMPSON (BIRMINGHAM, ALA.).—What about the symptoms of an ileitis which may be confusing? There may be an abscess formation up along the ileum.

CHAIRMAN MONTGOMERY.—Experimental work has shown that this is usually associated with a mesenteric adenitis and a regional ileitis.

DR. M. C. SOUTER (INDIANAPOLIS).—I have seen three cases recently which presented the picture of appendicitis, but on opening the abdomen the appendix was found normal and there was a mesenteric adenitis. These cases were all under four years of age. I did notice that the pain seemed more diffuse rather than localized in all three cases.

DR. BRENNEMANN.—An early diffuse pain is not usually sufficient for a diagnosis of appendicitis. What the case might be in infants, I do not know because I do not believe that we have any cases under one year of age.

DR. B. K. RUST (INDIANAPOLIS).—I have had one case of an infant, aged four months, who had a sudden onset of paroxysmal pain and I suspected an intussusceptions

tion from the history. I was able to begin my examination while the infant was asleep and felt fairly certain that no tumor was present, but I did find very definite and marked tenderness directly at McBurney's point. The infant began vomiting about four hours later. There was just a slight elevation in temperature and a white count of 12,000. The abdomen was opened eighteen hours after the onset of pain and an extremely gangrenous appendix was removed, which was pronounced extreme by the pathologist. Marked point tenderness was about my only lead in this case.

DR. J. B. BILDERBACK (PORTLAND, OREGON).—Pyuria is confusing in these cases, and why does it occur?

CHAIRMAN MONTGOMERY.—This is due to the close association of the tip of the appendix with the ureter. Never mind the pus if the case looks like an appendicitis.

DR. BILDERBACK.—I have seen appendicitis increase when there are many cases of chickenpox, measles and other contagious diseases.

CHAIRMAN MONTGOMERY.—This is true.

DR. RUST.—What anesthetic do you prefer in the cases of severe upper respiratory infections where you consider it also advisable to do an appendectomy?

CHAIRMAN MONTGOMERY.—I use a local anesthetic with whatever amount of ethylene gas is necessary to get relaxation.

DR. J. R. LEMMON (AMARILLO, TEXAS).—I have been interested in the difference between the incidence of appendicitis in the Americans as compared to the Chinese, Japanese and Filipinos. I do not remember seeing intussusception or appendicitis in thousands of patients from these races until after we had an epidemic of influenza, and then we had quite a few cases of appendicitis. I have seen that here, too. Is there a relationship?

CHAIRMAN MONTGOMERY.—There seems to be for we have noticed from year to year how with epidemics of upper respiratory infections there will be at one time numerous mastoids, or at other times a tendency for nephritis to develop, and then another epidemic will produce many cases of appendicitis following these respiratory infections.

DR. BRENNEMANN.—This specificity in various epidemics undoubtedly occurs. The work in Wisconsin must be considered where over a period of six years approximately 6,000 students were closely followed. It was found that there were eight times the number of cases of appendicitis occurring along with upper respiratory infections as compared to those without an upper respiratory infection. In case of suspected appendicitis we depend more on pain for diagnosis than muscular rigidity. When we find muscular rigidity, there is already peritoneal irritation. The appendix does not make much pain. I have known of a few cases in which abdominal glands have broken down and brought on a peritonitis. I do not think we can decide from the organisms found in the appendix what the original etiology was. We have found Levine tubes to be life-savers in peritonitis.

DR. C. F. SAWYER (CHICAGO).—We recognize two types of the disease, the infective and the obstructive. Either may occur alone early in the disease. In the infective type I do not believe that in older people 50 per cent come from infections in other parts of the body, as has been the opinion of Dr. Brennemann. In the obstructive type there is a lot more pain than in the purely infective type. The pediatrician's batting average is much superior to that of general practitioners.

The mortality rate is high and is increasing. I agree with Dr. Montgomery that those cases with an abdominal mass should be left alone. Also in our experience the mortality rate of those surgeons who come into the hospital from the outside is two and one-half times that of the surgeons on the staff of the hospital.

DR. F. S. CLARKE (OMAHA, NEBRASKA).—What is your attitude toward those cases which have been given castor oil on the third or fourth day?

CHAIRMAN MONTGOMERY.—A spreading peritonitis should be operated upon at once. A mass should be treated conservatively.

DR. CLARKE.—Do you remove the appendix if you operate during peritonitis?

CHAIRMAN MONTGOMERY.—Yes, if it can be easily removed.

DR. PERCIVAL NICHOLSON (ARDMORE, PA.).—In my experience most surgeons are too conservative in the treatment of early appendicitis; they do not operate soon enough. Do you get much aid from your pathologists, as a result of their pathological examinations of appendices?

CHAIRMAN MONTGOMERY.—I wonder if there is such a thing as chronic appendicitis. I do not believe there is. Of course I operate upon interval appendices.

DR. J. N. LANDE (SIOUX CITY, IOWA).—I had one case where an abscess drained out through the rectum. I wondered if it might be a case of suppurative glands, such as has been referred to.

DR. JOHN AULL (KANSAS CITY, MISSOURI).—I have always felt that acute appendicitis in children is nearly always secondary to an upper respiratory infection, just as is the case with acute catarrhal jaundice. I think perhaps one reason why our mortality rate is rising is that too many operations are performed because of vomiting and abdominal pain due to the onset of some other acute infection. To me vomiting does not even suggest appendicitis. Abdominal pain makes me think of the appendix. Tenderness on pressure strongly suggests appendicitis, but I depend chiefly upon muscular rigidity for my diagnosis and more particularly slight differences in muscular rigidity on the two sides.

DR. GUSTAV LIPPMANN (ST. LOUIS, MISSOURI).—We should teach students when to look for appendicitis; abdominal pain without diarrhea and with low fever should be considered appendicitis or peritonitis until it is proved otherwise.

DR. T. F. HUMPHREY (XENIA, OHIO).—Appendicitis, at times, comes definitely in epidemics. When these epidemics come on, there is much respiratory infection at the time.

DR. BRENNEMANN.—More than 50 per cent have a respiratory thing back of them. Notice the striking difference of opinion here between those men in pediatrics and the surgeons. We look at this thing from different viewpoints.

DR. A. F. SALOMON (OKLAHOMA CITY).—I had two patients operated upon for appendicitis in whom a ruptured graafian follicle was found.

CHAIRMAN MONTGOMERY.—I have operated upon some also when menstruation was beginning. These cases are perplexing.

DR. ROBERT E. CUMMINGS (CHICAGO).—I had three cases of appendicitis following chickenpox.

DR. J. H. DAVIS (CLEVELAND, OHIO).—Dr. Brennemann, what can you tell us about the relation of skin hyperesthesia to appendicitis?

DR. BRENNEMANN.—To me it does not mean anything.

CHAIRMAN MONTGOMERY.—I operated upon one allergic patient and found a normal appendix. Also in diabetes we may have severe abdominal pain.

DR. SAWYER.—What is the significance of these abdominal glands? Many times the appendix is definitely involved.

DR. BRENNEMANN.—I think it is a difficult thing to know the difference between normal and abnormal lymph glands.

DR. M. R. WOODWARD (SHERMAN, TEXAS).—I use barbiturates per rectum to quiet a child from one to three years of age who cries when the doctor attempts to make an examination.

CHAIRMAN MONTGOMERY.—Light anesthesia is advisable in these cases.

CLOSING REMARKS.—In closing this discussion I wish to say that I think we have all profited by the frank exchange of opinions in which everyone present has participated. I think you will agree with me that we all have a duty to perform in cutting down the present death rate from appendicitis in children. The pediatrician and the family doctor must realize and understand the importance of making a diagnosis at the earliest possible moment and they must consider the possibility of an inflamed appendix in every case of abdominal pain.

The surgeon who comes into the picture a little later must not only be able to diagnose appendicitis but must also be on the alert for the complications and various clinical conditions that the disease may present at this time. His judgment is probably more important than his technical skill. It is very apt to be founded upon his experience as Dr. Sawyer has said, and some of the deaths from this disease are undoubtedly due to operations performed by men with too little knowledge or experience in surgery. While time is an importance factor in the average case of appendicitis it is not such a grave emergency as to require operation at the hands of the first man available. The little extra time required to get a good experienced surgeon will probably be to the best interest of the patient in the long run.

Finally, we all have a duty as members of the medical profession to instruct and advise the public in regard to appendicitis so that we may obtain intelligent cooperation from the parents who, after all, must be regarded as the first line of defense.

DR. JOHN AULL, KANSAS CITY, MO.
DR. BYRON K. RUST, INDIANAPOLIS, IND.
Reporters.

## SIXTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

KANSAS CITY, MO., MAY 11, 1936

### Panel Discussion on Cyanosis in the Newborn

Chairman: Dr. A. Graeme Mitchell, Cincinnati.

Assistants: Dr. Fred L. Adair, Chicago; Dr. Barnet E. Bonar, Salt Lake City; Dr. Glenn E. Cullen, Cincinnati; Dr. Nicholas J. Eastman, Baltimore.

CHAIRMAN MITCHELL.—I am sure there are those in this audience who are quite certain that they know as much about this subject as those who are to participate in this panel discussion. I really hope that some of you know a little more.

We decided a while ago that the title of our discussion was somewhat confusing. In the first place, we should define in the beginning what a newborn infant is. Most of us in the panel decided we should discuss this subject of cyanosis and asphyxia in infants up to two weeks of age, because we wanted to say something about the late effects of asphyxia. We also felt that we were discussing something with which, in the final analysis, the general practitioner had a good deal to do. However, the obstetrician and pediatrician and probably also the biochemist must tell him some of the things to be done. In order to accomplish all this, we felt we should first, if possible, say what we do know or do not know about the causes of cyanosis and asphyxia both from the clinical point of view and from the point of view of the mechanism of their production.

There are certain confusing terms, which have been widely used, such, for example, as "acarbia." What does that mean? Some one has just handed me the latest edition of *Time*. In its column on medicine, it was reported that 400 stillborn babies were made to breathe by injecting a drug called alphalobelin into the vein of the umbilical cord when held upside down. It is not stated whether the cord was held upside down or whether it was the baby.

Apparently it is intimated that most of us have been negligent and have allowed many babies to die because we have not used the wonderful drug about which *Time* tells us.

There are many problems which we would like to elucidate and we must at least make the attempt. In order to do this, perhaps we should ask questions. Those which we considered were sent around to the various members of the committee and were about as follows:

1. What are the various causes of asphyxia and cyanosis in the newborn?

2. What is the mechanism of their production and does this differ when resulting from the several causes?

3. What starts the respiratory effort?

4. What is the value and what are the dangers of some of the methods employed in resuscitation? For example, does cutaneous stimulation do good and should it be employed? If so, under what circumstances?

5. What is the value of the tracheal catheter and is its use to be recommended for the general practitioner?

6. What is the status of inhalation of $CO_2$?

7. What are the advantages and disadvantages of various types of infant resuscitators and respirators?

I think that we might attempt, more or less informally in the beginning, to ask and answer some of these questions. We are not going to be formal. We have decided not to be particularly polite but to interrupt each other whenever we wish.

I shall ask Doctor Adair to start the discussion of this subject. Perhaps he would like to tell some of the causes of cyanosis or asphyxia in the newborn.

DR. FRED L. ADAIR.—Dr. Mitchell has referred to cyanosis in the baby which occurs in the first two weeks after birth, but we know it makes a lot of difference how mature the baby is when it is born. Obstetricians realize that some of their difficulties with the gaseous exchange of babies originate in utero before onset of labor, and a great many of the complications which lead to suffocation and asphyxiation in the baby arise during labor.

Among the factors affecting premature babies there are: the incomplete development of the lungs and their circulatory mechanism; the development of diseases and disorders which interfere with the gaseous exchange in the lungs after birth; and the failure of development of the neuromuscular mechanism which has to do with the establishment of respiration and is not manifested until after birth.

But, undoubtedly, the respiratory mechanism, as Doctor Eastman will conclusively demonstrate, operates in utero. The neuromuscular mechanism is functioning before birth but respiration is not established. Other complications which have to be considered are those that affect the gaseous exchange, the extraneous conditions which affect the lungs in various ways, and perhaps, that which affects the central nervous system and interferes with the neuromuscular mechanism.

I feel that probably intracranial bleeding and lacerations of the dural membranes are the best evidence we have of intracranial injury, but I believe there are a good many cases of intracranial injury which lead to the death of infants which are not manifested by evidence of either laceration or hemorrhage.

CHAIRMAN MITCHELL.—So far, we have gained an idea of some of the causes of asphyxia with which there is cyanosis in some instances. We have not been told what we are going to do about these different conditions, but there is a suggestion that there are dissimilar treatments for the several types of asphyxia and cyanosis. I wonder whether Doctor Bonar has anything to add to this classification, or whether he wishes to add other causes, and perhaps he might even give us some idea of what he does about these different types of asphyxia.

DR. BARNET E. BONAR.—I think we could more easily comprehend this vast subject if we made a diagrammatic scheme or outline of the mechanism of anoxemia. By the way, I think we should consider this whole subject as one of anoxemia rather than cyanosis or asphyxia. According to my figures, roughly about 85 per cent of all deaths in infants are associated to some extent with cyanosis or anoxemia in some form.

TABLE I

ANOXEMIA IN NEONATAL DEATHS

| | |
|---|---|
| Congenital debility (including prematurity) | 90% |
| Pneumonia | 100% |
| Birth injuries | 95% |
| Atelectasis | 100% |
| Congenital abnormalities | 50% |

In respect to the following outline of the mechanism of anoxemia in the newborn, I might say that I am not speaking of the intrauterine forms of anoxemia, although if we were to consider the placenta as the lungs in utero we could follow this same outline easily.

TABLE II

MECHANISM OF NEONATAL ANOXEMIA

| | | | |
|---|---|---|---|
| Respiratory System | Pulmonary Ventilation | Upper Air Passages | — Obstruction |
| | | Lungs | — Faulty Distention |
| | Arterial Exchange | Alveolar Wall | — Decreased Permeability |
| | | Hemoglobin | — Defective Hemoglobin |
| Circulatory System | Transportation | Heart | — Defective Force |
| | | Vessels | — Defective Circulation |
| | Tissue Exchange | Capillaries | — Stagnation |
| | | Tissues | — Defective Exchange |
| Central Nervous System | Medullary Centers | Respiratory<br>Cardiac<br>Vasomotor | — Depression |

Under the heading, respiratory system, pulmonary ventilation must be considered first. Naturally, we have to have normal air passages if an adequate amount of air is to get to the lungs. As far as the lungs are concerned, they must be properly distended if the organism is to reserve sufficient oxygen. Now, when we come to the next heading, the arterial exchange of the gases, the alveolar wall must be permeable in order that the proper gaseous exchange may occur. Under arterial exchange we must also consider the quality and amount of hemoglobin for not only must there be enough hemoglobin but also the hemoglobin must not be bound with some gas that is given off with great difficulty, such as carbon monoxide. However, in the newborn infant hemoglobin disturbances are found rarely.

The circulatory system in this outline may be divided into the transportation system, the heart and vessels, and that portion having to do with the tissue exchange of gases, the capillaries and tissues. Normal heart action must be maintained and the circulation of blood must not be interfered with. Otherwise, some of the symptoms found in asphyxia or cyanosis may appear. The vessels must be normal and the two systems, connected with the right and left sides of the heart, must not have abnormal communications which interfere with the oxygen supply to the tissues. For instance, if venous-arterial shunts or unaerated shunts are present we have difficulty for then the vessels carry improperly oxygenated blood to the tissues. In the tissues, changes occur which, I think, Doctor Cullen can tell you more about than I. The return of blood to the heart must be sufficiently satisfactory to prevent stagnation and asphyxiation of the tissues. The venous pressure must not be too great or stagnation will occur and the tissue exchanges will be interfered with.

Finally, there is the nervous system which, of course, has to do with the medullary centers, respiratory, cardiac and vasomotor. Under the various and several conditions encountered during and after birth, we often find these centers depressed and their depression in turn disturbs the normal functioning of the other systems that are outlined here.

From the next table (Table III) we can really consider the sites at which the normal interchange of gases may be broken up, that is, the actual contributing causes to cyanosis. All the instances of interference to the pulmonary ventilation through obstruction of the air passages may be divided into intrinsic or extrinsic causes producing pressure or obstruction from within or from without. These may be the result of foreign material such as mucus or amniotic sac contents, injury,

TABLE III

EXTRAUTERINE CAUSES OF NEONATAL ANOXEMIA

| | | |
|---|---|---|
| Obstructed Air Passages | Internal | Foreign Material<br>Trauma<br>Congenital Abnormalities<br>Infection |
| | External | Congenital Abnormalities<br>Tumors |
| Faulty Alveolar Distention | Internal | Atelectasis<br>Occlusion<br>Collapse<br>Rupture<br>Emphysema |
| | External | Weak Musculature<br>Intrapleural Pressure<br>Congenital Abnormalities |
| Decreased Alveolar Permeability | — | Pneumonosis<br>Edema<br>Exudate<br>Hyalin |
| Defective Hemoglobin | — | Anemia<br>Reduced Hemoglobin |
| Defective Cardiac Force | — | Failure |
| Defective Circulation | Unaerated Shunts | Cardiac<br>Respiratory<br>Peripheral |
| | Obstruction | Trauma<br>Infection<br>Congenital Abnormalities |
| | Vasodilation | Shock<br>Chilling |
| Depressed Medullary Centers | Intracranial Pressure | |
| | Chemical | Toxins<br>Drugs<br>Ch |
| | Shock | Anesthesia<br>Trauma |

congenital abnormalities, infection or tumors. While external causes such as an enlarged thymus or an infection of the tissues in the neck may be sufficient to cause interference with the passage of air into the lungs, most instances of obstruction are found within the various parts of the upper respiratory tract itself, mucus, congenital abnormalities or tumors.

Under the next heading is faulty distention of the alveoli. This comes about principally, I believe, through immaturity of the fetus whether it be prematurity or the

so-called congenital disability due to the toxemias of pregnancy or some other maternal disease. Immaturity itself favors faulty distention, either from inability of the alveoli to open up because of cohesion of the alveolar walls, atelectasis, or weakness of the respiratory muscles. Among the internal causes of faulty distention must be mentioned also occlusion with mucus or amniotic sac contents with alveolar collapse, rupture or alveoli which may occur from insufflation, or overdistention of some portions of the lung with subsequent inability of the adjacent alveoli to distend. Aside from weak musculature, intrapleural pressure from extravasation of blood or pleural transudates may be an external cause of faulty alveolar distention. Sometimes, however, as Doctor Adair has said, there are other extrinsic factors, mainly congenital abnormalities, such as eventration of the diaphragm, diaphragmatic hernia, or absence of some of the external muscles of respiration.

As far as the alveolar wall is concerned, we occasionally find an interference at this point, either through a fibrinous exudate or an edema of the wall which will not permit the gases to be interchanged, or as Rosenthal has spoken of occasionally, a hyaline membrane. This is found to have developed in some individuals, and when present, permeability is greatly interfered with.

We rarely see a deficiency in the hemoglobin of the newborn infant. Usually there is a sufficient amount of hemoglobin at birth and rarely is there such a thing as carbon monoxide poisoning or other abnormal combinations of hemoglobin.

Heart failure often develops from some of the causes I have mentioned, but as a primary cause of cyanosis it is rare. It is a late effect, a good example being found in the heart failure that occurs in the asphyxial crisis.

When we have an unventilated area of lung as in partial atelectasis, one of two things happens. Either the blood will go through the unaerated portion or it will be shut off from the involved area. If it goes through the undistended portion of lung, it will not take up oxygen, of course, and we have an unaerated shunt of venous blood to the arterial side. That is frequently a cause of some of the symptoms of asphyxia. But there is another thing that may happen at this particular point. The peripheral resistance in the lung will increase the pressure in the pulmonary blood vessel and cause something seldom mentioned, but which I think should be; namely, an increased pressure in the right heart with reopening of the foramen ovale and probably the ductus arteriosus. Peripheral shunts, such as the rare arteriovenous communications, may also interfere with the normal circulatory function.

Under the heading, obstruction, are listed briefly the several causes of more localized cyanoses. Trauma and infection usually produce only transient cyanosis through vascular dilatation, vasomotor paralysis causing stagnation in the capillaries with improper exchange of gases in the tissues. Congenital abnormalities, such as tumors, at times cause stagnation and cyanosis of a more permanent nature.

I think, under medullary centers, we might briefly mention intracranial pressure in which there occurs anemia of the brain from pressure upon it. This may be due to intracranial hemorrhage, depressed fractures, edema from trauma, tumors or hydrocephalus. Depression of the medullary centers may also occur from vasomotor paralysis, from chilling or following shock which is either a true vasomotor paralysis or possibly histamine shock from tissue injury.

Chemically, the medullary centers occasionally may be depressed as the result of toxins as in the neonatal infections. However, the most common chemical cause is the various drugs and inhalants used for reducing pain during delivery of the child.

CHAIRMAN MITCHELL.—Doctor Eastman, as you all know, has had a great deal of experience with this particular subject of asphyxia in the newborn, and has also done some significant work in relation to the causation and mechanism of the production of asphyxia and cyanosis and what ought to be done about it.

One of the questions I am hoping Doctor Eastman may answer or give some idea about is:

Why do these infants start to breathe or why do they not start to breathe after birth in those cases in which there is not obvious obstruction or something of that sort? Apparently the idea of most people who have attempted to make these babies breathe is that they are starting some new mechanism at birth. I think Doctor Eastman has some ideas about this, and I am going to ask him to discuss this particular phase of the subject.

DR. NICHOLAS J. EASTMAN.—While discussing these various causes of asphyxia neonatorum, it would seem worth while to consider for a few minutes, as Dr. Mitchell suggested, what happens normally in the few minutes after birth. What occurs in the absence of these interfering factors in the system of pulmonary ventilation? This, of course, brings up the question of the onset of respiration at birth. This subject has received an immense amount of attention, but it suffices to say here that theories based on physical stimulation as well as theories based on chemical stimulation fail to explain adequately the onset of respiration at birth.

Since the time of Ahlfeld in 1881, it has been suspected that fetuses make respiratory movements rhythmically in utero. This would seem logical and biologically sound since other organs such as the liver, kidneys, and heart function in utero, and it would seem singular if a system as important as that of pulmonary ventilation should suddenly start to function without previous preparation. While Ahlfeld thought these movements occurred, it was not until the present year that Snyder and Rosenfeld of our institution in Baltimore demonstrated them experimentally in rabbits, dogs, cats, guinea pigs, and monkeys. They are at present, I believe, able to demonstrate them through the abdominal wall in the human being.

I should like to present some motion pictures this afternoon showing these movements and at the same time emphasize the fact that this is not my work but that of Franklin F. Snyder, Associate Professor of Obstetrics at Johns Hopkins, and Morris Rosenfeld, Instructor in Pharmacology at the same institution.

They took rabbits at full-term pregnancy and under local novocaine severed the spinal cord to produce anesthesia of the lower limbs and abdomen, submerging the animal except the head in a bath of Ringer's solution at thirty-eight degrees. They then opened the abdomen under the Ringer's solution, exposed the pregnant horns of the uterus, and observed through the intact uterine wall these respiratory movements.

It is of interest to see occasionally as many as three fetuses breathing in utero at different rates, a circumstance which is difficult to correlate with any theory of the chemical onset of respiration at birth. In connection with such chemical theories, I should also like to call attention to the fact that at low cervical Cesarean section, performed under local infiltration anesthesia, it is possible to make a small incision in the lower part of the uterus, turn the baby around anteriorly and see it cry in utero. This again is a circumstance which is difficult to correlate with any chemical theory of the onset of respiration.

If a tracheal cannula is introduced into a rabbit and various gas mixtures given, it is found that they have a very definite effect upon these respiratory movements. When the uterine horn is incised and the rabbit fetus allowed to escape into the saline or Ringer's solution surrounding it, the placenta remaining intact, the fetus rolls about on the maternal abdomen and makes respiratory movements

for an hour or two. It then can be taken out of the bath and breathes and develops quite normally. In the moving picture we will show one of the rabbit fetuses under the Ringer's solution crawling around and breathing readily under the fluid.

CHAIRMAN MITCHELL.—Doctor Eastman, do these animals inhale any of the fluid?

DR. EASTMAN.—That is a question which is usually asked but it is very difficult to make any definite reply at the present time since further work is necessary.

DR. BONAR.—Can these movements be seen in the human?

DR. EASTMAN.—Doctor Snyder is working at that now. Ahlfeld put a tambour on the abdomen of pregnant women and made tracings of these movements, but subsequent attempts to corroborate this work have been unsuccessful. It is necessary to sit down and watch by the hour and that has not been done since the time of Ahlfeld.

I want to devote a minute or two to the practical significance of this viewpoint of the onset of respiration. It seems to me that it throws a greater burden upon the obstetrician. It is no longer his task to initiate the onset of respiration at birth by trying to simulate some complex chemical mechanism which is not well understood. On the other hand, it becomes the duty of the obstetrician to preserve a very delicate mechanism which is already in existence but which is easily disrupted. He will be more careful in the use of drugs which may have a harmful effect upon the fetus and which, as Doctor Snyder and Doctor Rosenfeld have shown, interfere with these movements. He will be cautious, in certain cases, in the use of barbiturates. He will possibly lessen his dosage of quinine; he will be careful in the employment of gas-oxygen anesthesia and will not raise the concentration above a 90:10 mixture, because concentrations of nitrous-oxide-oxygen stronger than 90:10 invariably produce marked anoxemia of the fetus and in experimental animals stop these movements. He will be more careful to prevent intracranial injury and forthwith the problem of asphyxia neonatorum becomes one more of prophylaxis, of helping these movements, which are already in existence, to continue.

CHAIRMAN MITCHELL.—It is a matter of history and record that Doctor Cullen has differed with Doctor Yandell Henderson in some of his ideas. Some time soon in this discussion we must discuss two or three things in the practical application of medicine in children who have asphyxia or cyanosis. I wonder what we have to think about the use of certain respirators, whether they are physiologic in their action, whether they do harm or good and who should use them. Also we have to discuss the matter of the use of inhalation. Should we give these infants oxygen or give oxygen and $CO_2$, and in what strength and under what conditions?

Doctor Henderson has said, "If you go to any biochemist he will say, 'this is just an acidosis and you cannot treat acidosis with carbon dioxide.'" I might ask Doctor Cullen how about that.

DR. GLENN E. CULLEN.—It seems to me, Mr. Chairman, that that remark puts the biochemist very much on the spot. I cannot help but feel that in the attempt to discuss the abnormal biochemical or physiological conditions that have to do with cyanosis in the newborn, too little attention has been paid to the determination of the immediate problem. In this discussion, then, Mr. Chairman, let us separate sharply the conditions that exist in the initial asphyxia of the newborn and those which develop after delivery. Let us then differentiate between

the treatment of the newborn child who suffers from lack of respiration, and the treatment which should be used when difficulties in respiration develop in the succeeding day or days. In searching the literature for information for this discussion, I have not found any other work as complete and convincing as that of Doctor Eastman. His work makes it clear that the immediate physiological need in the initial asphyxia at birth is oxygen. His work also shows that with the almost complete lack of oxygen there is, of course, definite change in the acid-base balance, and that with this change there is an unusually high tension of carbon dioxide already existing in the body. The immediate treatment, then, certainly centers around any method which will supply the oxygen to the tissues of these children. Since the $CO_2$ tension is already high, there would seem to be no need to increase further this high $CO_2$ tension in order to stimulate breathing. However, it does not follow that because there is already a high $CO_2$ tension the giving of a still higher $CO_2$ tension would not stimulate respiration or would be dangerous, because in the acidosis which occurs after ether anesthesia, the $CO_2$ tension, which is normally 45 mm. $CO_2$, goes up to 55 or 60 mm. $CO_2$ and yet the giving of sufficient $CO_2$ to increase the tension still further does result in a respiratory stimulus.

The possibility of damage from the use of $CO_2$ in stimulating respiration when it is really needed, seems to me to have an analogy in other conditions often met with in pediatrics. When a child is suffering from an alimentary irritation, we do not hesitate to temporarily deprive the child of food until we can get the alimentary tract back into a condition to handle food. The same is true of carbon dioxide. If a respiratory center for any reason, whether it be lack of oxygen or drug, has become insensitive to the stimulation which exists in that child's body, it would seem entirely logical to increase temporarily the stimulant by the administration of rather high $CO_2$ concentration. As soon as this initial stimulant has started respiration, it is then, of course, desirable to reduce the extra stimulation.

The answer to this question in this case is not one of reasoning but one of experimental evidence and I should like to ask Doctor Eastman if in those children, where he knows from analysis that the $CO_2$ tension is already 55 or 60, does he get as good results with oxygen alone as with oxygen plus $CO_2$?

DR. EASTMAN.—The question which Doctor Cullen raises brings one to the problem that has concerned a great many obstetricians and pediatricians in recent years, namely, whether carbon dioxide is the ideal stimulant to respiration at birth. For a great many years, Doctor Yandell Henderson has insisted on carbon dioxide. As a result of some studies that were begun in 1929 and which have been carried on since, I have accumulated certain evidence upon which I venture to take issue with Doctor Henderson. For the purpose of being brief, I have summarized this information on one lantern slide, which shows the oxygen content, the lactic acid content, the carbon dioxide tension, and the pH in various conditions at birth. It will be seen that the carbon dioxide tension in severe asphyxia is already extremely high and more carbon dioxide would seem not only superfluous but also possibly dangerous.

When we turn to the other question which Doctor Cullen mentioned, we have a different situation. We get away from the peculiar circumstances which exist immediately after delivery; and in the baby a few hours old, oxygen associated with carbon dioxide is probably logical since then, it seems to me, conditions are altered.

CHAIRMAN MITCHELL.—Could this be translated into the statement that in the newborn infants with asphyxia you do not need to give carbon dioxide under any conditions?

DR. EASTMAN.—If I may be permitted to do so, I should like to limit my statements to failure of respiration at birth, a condition with which after all the obstetrician is most directly associated and with which he has had the most experience. There I feel that carbon dioxide does not have a logical place and when given in mixtures of from 7 to 10 per cent, as is frequently done, may not only be superfluous but may prove harmful.

DR. CULLEN.—There is still one point, Doctor Eastman, that is not quite clear from what you have said. With those children where the $CO_2$ tension is 55 or 60, do you get as good results with oxygen alone as with $CO_2$ and oxygen?

DR. EASTMAN.—Clinically, it is very difficult to evaluate various gas mixtures. Often a baby is simply laid down and nothing is done to it because the condition of the mother demands immediate attention. Usually the baby starts to breathe perfectly well. It would require an enormous series of cases of asphyxia neonatorum to demonstrate definitely the most efficacious gases for initiating respiration at birth. I have not used carbon dioxide in excess of 4 per cent in the treatment of asphyxia neonatorum. I say 4 per cent because that is the concentration of carbon dioxide in the exhaled air, and I have often employed exhaled air in the treatment of this condition. However. that mixture can scarcely be considered stimulative.

DR. CULLEN.—Doctor Eastman's observation makes it necessary for us to think of the initial asphyxia at birth as primarily an oxygen lack and to plan future studies and treatment on that basis. Before we discuss the other division of our topic, the conditions that develop after birth, I should attempt to meet the criticism of the biochemist quoted by our Chairman from Dr. Yandell Henderson. I am very sorry that Doctor Henderson is not here so that the questions which he has raised in his many articles could be discussed with him. I should like to make clear how much admiration I have for Doctor Henderson's vigorous campaign for a logical method of resuscitation. There is no question that he should get the credit for introducing, universally, the use of carbon dioxide for carbon monoxide poisoning and for establishing a rational and proper administration of carbon dioxide and oxygen in this type of poisoning. He should also get credit for stimulating obstetricians and pediatricians to a more serious study of the problems of respiration of the newborn; but in giving him this credit we cannot refrain from insisting that the problems of respiration in the newborn are not questions of carbon dioxide only. These problems involve the interrelationship of carbon dioxide and of oxygen and of the whole electrolyte equilibrium of the fluids of the body and I think I am fair in saying that in his enthusiasm for the use of carbon dioxide, Doctor Henderson has lost sight of the physiology of respiration as a whole. He has introduced a term "acarbia," which I will not attempt to define for I think the concept incorrect, with the result of confusing the whole question of normal acid-base equilibrium of the body. My mission, today, is to attempt to make clear that in discussing respiratory distress we must consider the entire mechanism of respiration. This mechanism includes the absorption of oxygen by the lungs, the carriage of it by the blood to the capillaries, and the acceptance of it by the tissues. It includes the metabolism of oxygen to carbon dioxide, the neutralization of the carbon dioxide by sodium and potassium ions, the transportation of $CO_2$ as bicarbonate to the lungs, and the elimination of the carbon dioxide from the lungs by the reverse of the mechanism by which oxygen is absorbed. This mechanism involves to a great extent the change in the acid nature of hemoglobin with oxygenation and deoxygenation which, in ordinary respiration, accounts for 90 per cent of the transport of carbon dioxide from the tissues. One would think from Dr. Yandell Henderson's discussions that the only respiratory stimulant is

carbon dioxide and that the alkalies in the body move back and forth from tissue to blood in some mysterious manner. This question has been studied for many years and most of us, who have been interested in chemical physiology of the blood, have thought that it is fairly well determined that it did not make any difference whether carbon dioxide or lactic acid or hydrogen ion was the immediate cause of this stimulus to the respiratory center so long as there was a change in the reaction of the fluid bathing the cells of the respiratory center. I have been using the term "acid-base balance" in an attempt to dodge the words "acidosis" and "alkalosis." If it were possible for any one biochemist or physiologist to attain sufficient prestige or persuasiveness to remove the terms "acidosis" and "alkalosis" from present-day usage and to have the conditions which these terms should represent expressed in terms of acid-base balance, that man could die happy, knowing he had done something for medicine. Since that is probably not possible, we can only keep on attempting to use these terms intelligently. To do that we must recognize that the acid and alkaline constituents of body fluid exist in equilibrium which varies in the normal individual between two very definite, well-established limits. When there is an excess of normal acids, such as carbon dioxide or lactic acid, or when there are sufficient amounts of abnormal acids, such as occur with faulty metabolism of the fat in diabetes, we have a condition which may be termed "acidosis." This may be measured in terms of lowered $CO_2$ content or of increased hydrogen ion concentration or of both. Whenever there is an excess of alkali in relation to acid either due to ingestion of abnormal amounts of alkali or to loss of acid in the system, as in vomiting, or to lowered tension of carbon dioxide as in excessive ventilation, the acid-base balance is disturbed toward the alkaline side and we have a condition of "alkalosis." It is not safe, however, to use these terms unless we express the condition in a quantitative manner precisely as we state in a febrile condition the extent of temperature change. The continued use in a careless manner of the term "acidosis" to describe a condition where there are ketone substances in the urine or when some one has an upset stomach cannot be deplored or condemned too much. Further, I cannot overemphasize one of the fundamental points of view which has developed in studying such condition in young children. That is, it is not possible for even the best clinicians to determine by ordinary clinical observation whether or not a child, and especially an infant, has an "acidosis" or "alkalosis." This is much more true for pediatric medicine than for adult medicine. After many years of cooperation with medical colleagues in various hospitals, I thought I could tell, fairly accurately, whether or not an adult was suffering from acidosis or alkalosis. Now, however, I know from experience in the Children's Hospital in Cincinnati (and I think you will admit that we have some fairly good clinicians there) that none of us can tell, without an examination of the blood, the condition of the acid-base balance of the blood. Still more important, even if by luck we make a correct guess as to which abnormality, if any, exists, we cannot with any safety prescribe adequate treatment without quantitative data upon which to base our theory.

When we once get this clear-cut and really simple concept of acidosis and alkalosis ingrained in the medical consciousness, then we can logically discuss whether or not the conditions in which we are now interested involve these disturbances of acid-base balance. There is no question at all that there is much more actual alkalosis, in the correct use of the term, in infants and young children than has been thought to exist. We have seen many children referred to us as problems of acidosis which, in reality, were acutely ill with an alkalosis, and we have been able to treat many of them with most happy results. But we would never have dared to treat a child with an acute alkalosis unless we knew by careful analysis exactly how severe was the condition. In other words, we have no right to treat

any condition as a disturbed acid-base equilibrium unless we know that there is such a disturbance and we have no right to treat with specific therapy unless we can treat on a quantitative basis.

I hope some of you will stop and ask yourselves if you really know what you are saying before you again use the term "alkalosis" or "acidosis" or prescribe treatment for such a supposed condition.

CHAIRMAN MITCHELL.—Recently we have heard a good deal of criticism of some of the older methods of resuscitation where the newborn was played football with for a while. I wonder whether we had not better have some discussion of that. What about the matter of turning the baby upside down in relation to the possibility of increasing the danger of intracranial hemorrhage? Can those methods which have been used so widely for so many years actually do harm? The statement has been made, for example, that cutaneous stimulation does these babies no good. Clinically, it seems to do so under certain conditions if there is obstruction. What about tracheal catheter? Is that something we could or could not use? What is your experience, Doctor Adair?

DR. ADAIR.—For many years I have used oxygen and since coming to Chicago from Minneapolis have tried out various mixtures of carbon dioxide and oxygen clinically. Personally, I am convinced from clinical observation that Doctor Eastman is correct in his conclusions from experimental work. But I would also like to emphasize again and again the fact that many of these babies who do not breathe properly have something else radically wrong with them.

In order to convince you of that, I would like to give some data based on autopsy experience with practically one thousand cases in which 103 babies were born alive, where there was a heart beating and yet it was not possible to establish respiration. There was evidence of birth trauma present in forty-nine; a major anomaly in twenty-two; prematurity under seven months in three; atelectasis in four; four not diagnosed, with sixteen cases of suffocation and aspiration in which no other cause was found.

To summarize briefly my opinion relative to resuscitation, I would say it is important first to remove mucus, amniotic fluid, etc., from nasal and pharyngeal passages so that air may enter easily and obstruction of bronchi and alveoli does not occur. This may be done by holding the infant by the feet with head dependent, supporting the shoulders, and either milking out the content of the trachea and mouth or gently sucking it out with a tracheal catheter or bulb suction. When a baby once starts to breathe and the reflex action is established, there is little danger of aspiration into the trachea or bronchi.

The second main objective is to initiate respiration by artificial methods, various measures of cutaneous stimulation, snapping the nose or perhaps the mouth in the absence of something better, or gently rubbing the back with a rough cloth or something of that kind to stimulate respiration in the milder cases; the overcoming of anoxemia with oxygen; and (questionable) the stimulation of the respiratory center with $CO_2$ and oxygen. Proper temperature of the baby must be maintained while respiration is being established.

I should like to emphasize the importance of maintaining the proper temperature from the moment of birth on, and second, the importance of the frequent administration of oxygen. I should like also to emphasize again the necessity of using gentle procedure so that no additional lesion is produced or any existing one exaggerated and no additional trauma is created.

CHAIRMAN MITCHELL.—Would you say something about the use of infant respirators?

DR. ADAIR.—We have tried a number of different infant respirators. We have usually been so well satisfied and have relied so much upon the simpler procedures we have used that we hesitate to change. Also, although we have tried respirators on a series of cases, we are a little afraid of some of them, especially in teaching our students and internes certain of these methods, because we feel some of them are intrinsically dangerous. Furthermore, many of our students and many of our internes who go through our institutions are going to practice obstetrics where such an apparatus is not going to be available, both in the home and in hospitals which are not equipped with it. We think the simpler the procedure the better.

I might say that in some cases we have simply used the tracheal catheter with a Y-shaped tube connected with the oxygen tank and have allowed the flow of oxygen to come in with intermittent pressure over the free end of the tube, thus alternately injecting and releasing the oxygen. It is a simple device that can be controlled with this simple valvelike action so that pressure does not become excessive.

There is a very real danger of traumatizing babies from the introduction of instruments into the trachea, a danger of producing expansion with rupture of the alveoli of the lungs and danger of forcing material which may have been aspirated into the trachea or bronchi to a lower level in the lungs.

CHAIRMAN MITCHELL.—I think, Doctor Bonar, you have figures which show that 85 per cent of babies are stillborn in homes where the various types of apparatus are not available. A question which has been sent up here is: Can you tell us something more about the matter of anesthetics or analgesia, the matter of morphine, for example, and other things given to the mother? What effect do these have? It has been intimated they may have a direct effect.

DR. BONAR.—As Doctor Eastman has shown, there is no doubt but what morphine has a detrimental effect on the respiratory center of the newborn infant, and the barbital series in general have the same effect. We must be cautious in the use of these preparations and if we must use them, we should have the patient under continuous observation in order to be prepared to care for an asphyxiated baby in case of delivery before the anticipated time.

I think Dunham and Clifford have shown it is safe to use morphine or dilaudid up to three hours before delivery without any particularly deleterious effect upon the infant. But we do not always know whether the patient is going to wait for three hours, and if she does not there is impending danger of asphyxia. If that happens, one should immediately be prepared ahead of time, that is, be ready for an asphyxiated child.

One could not discuss the subject of anesthesia in childbirth in the two and one-half minutes allotted by the chairman. I feel we have been treading on dangerous ground in respect to these preparations. I think it pernicious, this habit that some men have of trying one of these drugs in a small series of cases and rushing into print to state that it is safe for the mother and that the baby is not asphyxiated. So far we have had no good criterion to determine whether or not the baby is asphyxiated. I think the work of Shute regarding the clinical manifestations of narcosis in the newborn is one of the best I have seen in this respect. All obstetricians should read it. Another pernicious habit is that of some men connected with well-manned and well-equipped lying-in hospitals advocating for general use some of these preparations which, after all, demand closer attention than can usually be paid the patient during labor in less sumptuous hospitals or in the home. Measures of this sort cannot be labeled innocuous for they all carry some hazard to both mother and child.

Furthermore, we have no simple clinical criterion as to when a child is free from anoxemia. In this respect I am not speaking of children immediately after birth but later on, that is, in the early days of life when pulmonary ventilation should be increased in extent.

Is it not possible that some of the anesthesias and analgesias may cause trouble through mild depression of the respiratory tract with subsequent faulty ventilation over a period of time? That is a question I cannot answer but I have always felt there is that danger and that brings up the question of the late effects of anoxemia in the child. I have agreed with Doctor Eastman for several years that the child at birth is acidotic. I think that comes about naturally through an increased amount of carbon dioxide in the blood. Once respiration has been established in a partially ventilated lung, it may develop the so-called physiologic shallow breathing which may wash out carbon dioxide and possibly produce what we might call an alkalemia.

In those particular cases where there is a high carbon dioxide content of the blood, it seems to me there is little indication for carbon dioxide but in those cases, the few that we might have, where there is a deficiency in the carbon dioxide in the blood it might be possible to help respiration by the use of carbon dioxide and oxygen.

Doctor Mitchell has asked what to do in the home or that group handled by the general practitioner. It seems to me there is a rule of thumb he can work out that is simple and does not need any fanciful equipment. If the patient is in a hospital, try oxygen first and if it does not succeed, try carbon dioxide and oxygen. There is no harm in it and if it helps out more than the oxygen, use the carbon dioxide oxygen mixture.

In the home other measures may be necessary. So far as insufflation is concerned, I think perhaps the mouth-to-mouth breathing could be better protected. It is dangerous from the point of view of distention of the alveoli. In using the Mackenzie mask, which is very small, the operator blows into the mask and the air is reduced in pressure so it will not be dangerous to the child, that is, the air will not overdistend the alveoli. At the same time, there is an opportunity in that instrument for the use of a little aromatic spirits of ammonia. This is an easy way for the physician to give oxygen and carbon dioxide. If he does not want to give carbon dioxide he can open his mouth, fill it with air, and blow into the mask without breathing out.

Tracheal catheterization is dangerous and I cannot feel that it can be used by every one as it will not be used properly in many instances. I noticed recently in the *Journal of the American Medical Association* an article about the use of the Flagg instrument. The writers of that article mention the fact that they have had a few injured babies. In a few the larynx has become edematous. I do not think the average person would be capable of using that instrument safely. It is not easy to insert a tracheal catheter into the trachea and since they are made of linen and are stiff, they can traumatize the larynx. The other method of modified mouth-to-mouth breathing would probably be satisfactory in the majority of instances and certainly more adaptable and safer for home conditions.

In regard to turning the baby upside down, I have never felt it necessary to do this. When the baby is turned upside down, we increase the brain volume and pressure, and one should be very cautious about doing this. I think it far better to first aspirate the mucus with a soft-nosed rubber bulb or ear syringe, which, by the way, is better than the mechanical aspirator for the negative pressure is about right and not too great. After the mucus has been aspirated the infant's head may be lowered a little.

CHAIRMAN MITCHELL.—Doctor Cullen, in your discussion of the chemical factors associated with asphyxia at birth, you did not go on to the cyanosis that develops after birth.

DR. CULLEN.—It is apparent that all of us are in agreement with Doctor Eastman in regard to the importance of the use of oxygen for asphyxia and cyanosis at birth. We cannot say for the cyanosis which develops after birth that the only disturbance is one of acid-base balance. Even though we may find such a disturbance, experience has taught us that changes of acid-base balance are not usually primary causes of abnormal conditions but are secondary. Further, even when we recognize that abnormal acid-base conditions exist which should be treated in order to prevent consequences that may be more serious than the initial condition, we should not become so enthusiastic about finding one abnormal condition that we forget that there are probably other equally important abnormalities. We must search for an understanding of the complete story. So, in these conditions of cyanosis which have developed in children after birth, and in which probably the most outstanding symptom is that of respiratory distress, we must realize that we may have an accumulation of difficulties such as slightly impaired circulation, a low temperature, a slight hemorrhage, or slight amount of fluids or other débris in the lungs, any one of which in itself may not be sufficiently severe to cause acute respiratory distress but which, operating together, have a cumulative effect that is dangerous.

No discussion of abnormal chemical conditions of the body in the newborn could be complete without mentioning two fundamental differences between the newborn and the adult human. The first of these is that the water mechanism of the infant's tissue is much more labile than in the adult and that loss of tissue fluid from any cause may bring about much more serious damage to the tissue than does a proportional loss of fluid in the adult. The second factor is that time is of much more importance in children than in adults.

It may seem naïve for me to emphasize these two points to an audience of pediatricians, but let me remind you that in general the application of fundamental physiologic chemical facts to children are based upon observations and experiments mainly carried out with normal adult human beings or upon adult laboratory animals. Although I do not know yet how to gather facts that can be expressed in sound mathematical terms, I am sure that when we carry over our experimences of abnormal acid-base conditions in the adult to children, we must add to other considerations that of time. For example, an acidosis not severe enough to injure permanently an adult even though it persists for a considerable period of time, may cause permanent damage to a child within a few hours.

CHAIRMAN MITCHELL.—I have the duty of trying to summarize what has been stated. It seems to me we have got two or three things fairly clear. In the first place, we cannot use the terms "asphyxia" and "cyanosis" as symptoms without qualifications any more than we can the term "edema." These may also be symptoms of different disturbances. Asphyxia and cyanosis in the newborn may be caused by a number of different things, which could perhaps be divided into the extrauterine and intrauterine groups. Certainly, we must first find, if possible, whether there is some mechanical obstructive factor. We have to think definitely of some of the other causes which need a different type of treatment. For example, intracranial hemorrhage puts a different aspect on the subject treatment of cyanosis.

I think that the obstetrician told us that one of the first procedures was to look for obstruction in the air passages, which frequently is caused by accumulation of secretion or mucus in the nose or throat. Those should be removed before attempting to do anything else. We must be careful not to use too much force, because this may possibly do the infant harm.

Probably, some of the older methods did more harm than good and they should be discarded, although I gather from the discussion and from reading that the obstetricians themselves are not willing to give up entirely some of the more gentle methods of artificial respiration.

I think that the work Doctor Eastman has shown us makes us think that after all we are not attempting to establish something new in respiration but rather attempting to assist something which is physiologic and automatic. Perhaps having done that, we do not need to do much more. Doctor Eastman makes the statement that often the best thing that can happen to the baby is that everyone else is too busy to bother about it so that it may have the opportunity to breathe itself.

I do not feel that there has been sufficient emphasis concerning the factor of giving anesthesia to the mother, which Doctor Bonar has stressed in this discussion. A matter which has not been touched upon is alphalobelin. I think Doctor Eastman agrees with Alan Moncrieff's published opinion that it is a very dangerous drug and it might be possible that we will find the article in *Time* to be entirely wrong.

DR. EASTMAN.—I have seen two deaths following injection of this drug, both preceded by convulsive seizures. The first one I thought was a coincidence but the second I felt was more than this.

CHAIRMAN MITCHELL.—We all agree that there is a difference in the treatment of asphyxia at birth and of respiratory distress that develops after birth.

I do not know how to summarize the matter of whether we should or should not use inhalation of carbon dioxide with oxygen. It seems clear that in the asphyxia at birth oxygen, either pure or as air, is most important. For the respiratory distress that develops after birth, it would appear that $CO_2$ may, in some instances, be of great value, since $CO_2$, judicially used in these cases, is probably not harmful and the logical procedure would be to give the infant the chance to show whether or not $CO_2$ benefits him. We certainly cannot now consider that the question is other than in the experimental stage and I cannot see how we can ignore Doctor Cullen's insistence that we determine the condition of acid-base balance before we treat for supposed acid-base disturbances.

In speaking for the group participating in this discussion, I think it fair to state that although we have not been able to answer finally the many questions that have been brought out we all have a much clearer concept of these various problems and their interrelation than we had before.

# Academy News

The next annual meeting of the Academy will be held at the Waldorf-Astoria Hotel, New York City, June 3, 4, and 5, 1937.

### Michigan Meeting, July 17, 1936

The Michigan Members of the Academy met July 17, 1936, at the Detroit Boat Club on Belle Isle, Detroit, Michigan, for dinner and the summer meeting. Twenty-two of the forty-five members in Michigan were present, with especially good representation of the out-state members.

Dr. Lillian Smith, one of the Michigan Members, who is Director of Maternal Welfare and Public Health Nursing of the State Department of Health, outlined the proposed program for the utilization of Federal Funds in Michigan under the Social Securities Act—Sections IV and V.

Dr. T. B. Cooley opened the discussion of the program. Dr. L. Fernald Foster, a member of the committee representing the Michigan Members of the Academy and also chairman of the Public Relations Committee of the Michigan State Medical Society, outlined the sentiment of the profession and discussed some of the problems involved.

After a lengthy discussion, the program as outlined by Dr. Smith with the additional suggestions and recommendations of the members, particularly with reference to the importance of providing postgraduate teaching in the areas to be covered by the program, was endorsed.

The Committee on Postgraduate Education through its chairman, Dr. J. Johnston, reported the success of the second annual three-day postgraduate course given in April in Detroit. Sixty-six physicians from Michigan, Ohio, and the Province of Ontario attended. Two-thirds of this group came from an area of more than thirty miles distance from Detroit.

Dr. Fred Miner discussed the advisability of the Michigan Members adopting a resolution requesting the State Medical Society to adopt the report of the Committee of the Academy covering prophylactic immunization.

It was reported that in all counties of the state in which members of the Academy resided, at least one member of the Academy was represented on the Medical Filter Committees appointed by the Judges of Probate to assist in the administration of the Afflicted Child Act.

The next meeting of the Michigan Members of the Academy will be held September 23, 1936 at Detroit at the time of the Annual Meeting of the Michigan State Medical Society.

# News and Notes

Dr. Robert A. Strong, Professor of Pediatrics, Tulane University, began a course of lectures in Pediatrics on July 6, 1936, at Clarksdale, Mississippi. This course of lectures is open to physicians of Mississippi and is to be given in different sections over the state. It consists of five lectures a week on important phases of Pediatric practice.

These lectures are sponsored by the Mississippi State Medical Association, the State Hospital Association, and the State Board of Health; also, by Tulane University School of Medicine and the Graduate School of Medicine. The Mississippi State Pediatric Society has approved these lectures and is heartily cooperating with the other organizations. The following committee on Postgraduate Medical Education is in charge of the course. Dr. Harvey F. Garrison, President, Mississippi State Medical Association; Dr. J. W. Lipscomb, President, Mississippi State Board of Health; Dr. Felix J. Underwood, Mississippi State Health Officer; Dr. H. W. Kostmayer, Dean, Tulane University Graduate School of Medicine; Dr. C. C. Bass, Dean, Tulane University School of Medicine; Dr. Leon S. Lippincott, Secretary, Mississippi State Hospital Association and Dr. W. H. Anderson, Editor, *Mississippi Doctor*, official organ of the Mississippi State Medical Association.

At the meeting of the **Mississippi State Pediatric Society** which was held in Jackson, the following officers for 1936-1937 were elected:

Dr. Harvey F. Garrison, Jackson, Miss., President
Dr. John K. Bullock, Jackson, Miss., Vice-President
Dr. Guy C. Jarratt, Vicksburg, Miss., Secretary-Treasurer

Final notice is given by the **American Board of Pediatrics** to all pediatricians who wish to be certified by the Board, who belong in Group I, that after September 1 an examination will be required of all applicants in this group. This group consists of physicians who have been engaged in Pediatrics for ten or more years and are subject to certification without examination. Also, the fee for certification advances from $20.00 to $30.00 on the above date for all applicants, no matter to what group they belong. If you have not already made application, attend to this matter at once.

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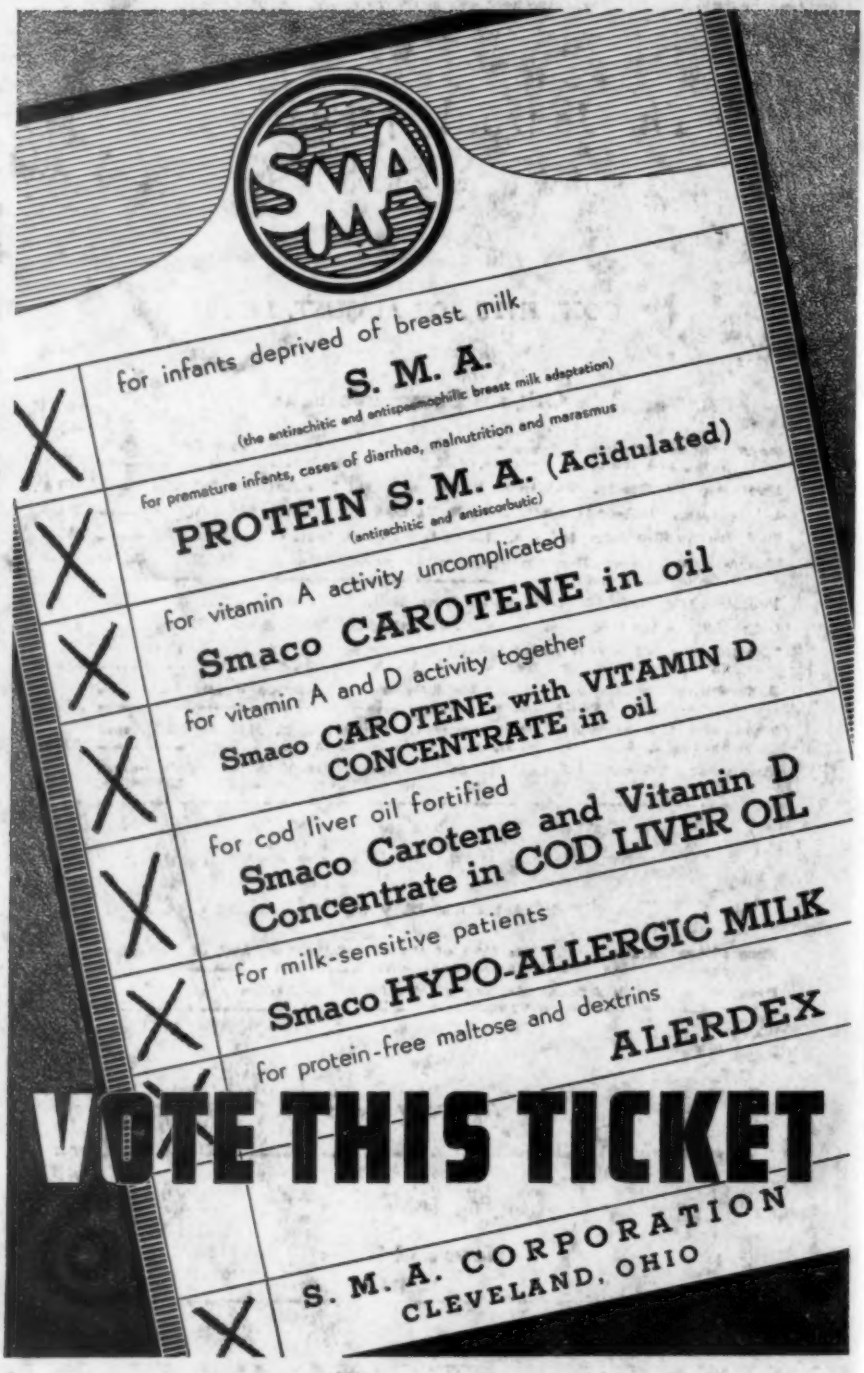
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